COUNTWAY LIBRARY
HC 3IIQ 8

OFFICIAL JOURNAL OF

ARIZONA MEDICAL ASSOCIATION · CALIFORNIA MEDICAL ASSOCIATION · DENVER MEDICAL SOCIETY · IDAHO MEDICAL ASSOCIATION · NEVADA STATE MEDICAL ASSOCIATION · NEW MEXICO MEDICAL SOCIETY · UTAH MEDICAL ASSOCIATION · WASHINGTON STATE MEDICAL ASSOCIATION · WYOMING MEDICAL SOCIETY

ST #4

DISPLAY SHELVES

The Western Journal of Medicine

VOLUME 170 • NUMBER 1 JANUARY 1999

EDITORIAL

9 On Being Editor
LH CLEVER

ARTICLES

11 Simultaneous Pancreas-Kidney Transplantation: An Overview of Indications, Complications, and Outcomes
CE FREISE, S NARUMI, PG STOCK, and JS MELZER

19 Research Interests of Physicians in Two Practice-Based Primary Care Research Networks
MS CROUGHAN-MINIHANE, DH THOM, and DB PETITTI

25 Relationship Between Earlier and Later Mammography Screening—California Medicare, 1992 Through 1994
JD PARKER, F SABOGAL, and T GEBRETSADIK

28 Mental Illness in Elementary-School-Aged Children
A CHABRA, GF CHÁVEZ, and ES HARRIS

35 Internal Medical Residents' Ability to Diagnose and Characterize Major Depression
MA MEDOW, SJ BOROWSKY, S DYSKEN, SD HILLSON, S WOODS, and TJ WILT

41 Nonsurgical Causes of Pneumoperitoneum
RA MULARSKI, ML CICCOLO, and WD RAPPAPORT

ALERTS, NOTICES, AND CASE REPORTS

47 Cocaine-Induced Intestinal Ischemia
MA WATTOO and O OSUNDEKO

49 Potentiation of Warfarin Sodium by Amiodarone-Induced Thyrotoxicosis
KA WOEBER and I WARNER

51 Persistent Hiccups Induced by Dexamethasone
J ROSS, M ELEDRISI and P CASNER

LESSONS FROM THE PRACTICE

53 Alone
WE BYRD

55 Saying No
V MAIZES

OTHER FEATURES

4 Continuing Medical Education Activities
57 Poetry
58 Classified Advertising
60 Instructions for Authors

Detailed Table of Contents: 2, 3

THE FRANCIS A. COUNTWAY
LIBRARY OF MEDICINE
BOSTON, MA

JAN 20 1999

Affiliated Clinical Investigation Societies: the Western Association of Physicians; the Western Society for Clinical Investigation; the Western Section, American Federation for Medical Research; the Western Society for Pediatric Research; the Western Region, Society for Investigative Dermatology

Full text, free access.

– Fully searchable archive –

– 150 topic collections –

– Customised email alerting –

– Rapid responses –

– Enhanced articles –

– Extra news stories –

– Direct Medline access –

– Jobs, courses, and careers –

And we don't ask you to pay, subscribe, register, provide passwords, or fill in interminable online questionnaires.

www.bmj.com

THE FRANCIS A. COUNTWAY
LIBRARY OF MEDICINE
BOSTON, MA

The Western Journal of Medicine®

SINCE 1902

221 MAIN STREET • SAN FRANCISCO, CALIFORNIA 94120-7690
TELEPHONE (415) 882-5177; FACSIMILE (415) 882-3379; E.MAIL rstraube@bmjgroup.com

JAN 20 1999

LINDA HAWES CLEVER, MD, *Editor*
EDWARD D. HARRIS JR, MD, *Associate Editor*

CATHERINE NANCARROW, *Editorial Manager*
NEIL POPPMACHER, *Production Manager*
RUTH STRAUBE, *Business Manager*

editorial communications to CATHERINE NANCARROW • business communications to RUTH STRAUBE

Official Journal of the Alaska State Medical Association, the Arizona Medical Association, the California Medical Association, the Denver Medical Society, the Idaho Medical Association, the Nevada State Medical Association, the New Mexico Medical Society, the Utah Medical Association, the Washington State Medical Association, and the Wyoming Medical Society.

Affiliated Clinical Investigation Societies: the Western Association of Physicians; the Western Society for Clinical Investigation; the Western Section, American Federation for Medical Research; the Western Society for Pediatric Research; the Western Region, Society for Investigative Dermatology.

SPECIAL EDITORS

Special Editor for Arizona
Marshall B. Block, Phoenix, Ariz

Special Editor for Denver
David Shander, Denver, Colo

Special Editor for Idaho
E. R. W. Fox, Coeur d'Alene, Idaho

Special Editor for Nevada
Anton P. Sohn, Reno, Nev

Special Editor for New Mexico
I. Brian Taylor, Carlsbad, NM

Special Editor for Utah
C. Basil Williams, Salt Lake City, Utah

Special Editor for Washington
David Hopkins, Federal Way, Wash

Special Editor for Wyoming
Joseph P. Murphy, Casper, Wyo

ASSISTANT EDITORS

Clinical Investigation
H. Benfer Kaltreider

Health and Public Policy
Ralph Crawshaw

International Health
Anvar Velji

Lessons From the Practice
Stephen J. McPhee
Jonathan E. Rodnick

Medical Staff Conferences
Nathan M. Bass

Poetry
Margaret Kaufman

Primary Care Medicine
Stephen J. McPhee
Terrie Mendelson

Radiologic Cases
Jonathan M. Levy

EDITORIAL BOARD

Editor Emeritus
Malcolm S. M. Watts, San Francisco, Calif

Anesthesiology
Carol Lake, Sacramento, Calif

Biostatistics and Epidemiology
Virginia L. Ernster, San Francisco, Calif

Cardiac and Thoracic Surgery
Norman E. Shumway, Stanford, Calif

Dermatology
Clifton R. White Jr, Portland, Ore

Emergency Medicine
William A. Boehm, Alamogordo, NM

General and Family Practice
Norman Kahn, Kansas City, Mo
Thomas E. Norris, Seattle, Wash
Joe Schoeber, Casper, Wyo

Internal Medicine
Albert Deisseroth, Houston, Texas
Alan Fogleman, Los Angelas, Calif
Patricia Gabow, Denver, Colo
John H. Holbrook, Salt Lake City, Utah
Philip Hopewell, San Francisco, Calif
Irwin J. Schatz, Honolulu, Hawaii
Walter E. Stamm, Seattle, Wash
Reginald Strickland, Albuquerque, NM
Stephen I. Wasserman, San Diego, Calif

Neurology
Robert Collins, Los Angeles, Calif
John Greenlee, Salt Lake City, Utah
Leslie Wiener, Los Angeles, Calif
Earl Zimmerman, Portland, Ore

Neurosurgery
George A. Ojemann, Seattle, Wash
Robert F. Spetzler, Phoenix, Ariz

Nuclear Medicine
Jerold M. Lowenstein, San Francisco, Calif

Obstetrics and Gynecology
Daniel Mishell Jr, Los Angeles, Calif

Occupational Medicine
Linda Rosenstock, Washington, DC

Ophthalmology
Sandy Feldman, La Jolla, Calif

Orthopedics
Thomas DeCoster, Albuquerque, NM

Pathology
Ronald Weinstein, Tucson, Ariz

Pediatrics
Allen W. Mathies Jr, Pasadena, Calif
Diane Wara, San Francisco, Calif

Pharmacology
Rubin Bressler, Tucson, Ariz

Physical Medicine and Rehabilitation
Julie G. Madorsky, Pomona, Calif

Preventive Medicine and Public Health
Joseph L. Lyon, Salt Lake City, Utah

Psychiatry
J. Christian Gillin, San Diego, Calif
Lewis Judd, La Jolla, Calif

Radiology
Gary Glazer, Stanford, Calif
Michael L. Manco-Johnson, Denver, Colo
Albert A. Moss, Seattle, Wash

Surgery
Haile T. Debas, San Francisco, Calif
Alex G. Little, Las Vegas, Nev

Urology
Linda Shortliffe, Stanford, Calif

Senior Members at Large
Thomas Elmendorf, Davis, Calif
Edgar Wayburn, San Francisco, Calif

ADVISORY BOARD, CLINICAL INVESTIGATION

Brian A. Cason, San Francisco, Calif
John Christenson, Salt Lake City, Utah
Kari Connolly, San Francisco, Calif
Bruce W. Goldberg, Portland, Ore
Philip Goodman, Reno, Nev
Roy Jones, Albuquerque, NM
Howard Lien, Tucson, Ariz
Barbara M. Lippe, Los Angeles, Calif
Michael W. McDermott, San Francisco, Calif
Jeanette Mladenovic, Denver, Colo
Kenneth M. Moser, San Diego, Calif
James C. Orcutt, Seattle, Wash
John Owings, Sacramento, Calif
Robert Robbins, Stanford, Calif
Henry Rosen, Seattle, Wash
Mary H. Samuels, Portland, Ore
George A. Sarosi, San Jose, Calif
Jeffrey Saver, Los Angeles, Calif
David Schriger, Los Angeles, Calif
Jack H. Simon, Denver, Colo
Peggy Sue Weintrub, San Francisco, Calif
Owen M. Wolkowitz, San Francisco, Calif

DISPLAY ADVERTISING INFORMATION

CONTACT: Alan Walker, BMJ Publishing Group, BMA House, Tavistock Square, London WC1H 9JR, UK • (+44) 171-383-6226/FAX (+44) 171-383-6556. Email: awalker@bmj.com
Advertisements—The journal is published the second week of the month. Display advertising must be received no later than the first of the month preceding issue. Advertising rates will be sent on request. Acceptance of advertising is contingent upon approval by the Publisher.
The journal reserves the right to reject any advertisement.

CLASSIFIED ADVERTISING

CONTACT: Ruth Straube, The Western Journal of Medicine, 221 Main St. San Francisco, CA 94120-7690 • (415) 882-5177/FAX (415) 882-3379.

SUBSCRIPTION INFORMATION

The subscription price is $70 per year and $130 for 2 years in the United States and Canada (US funds); $85/$160 in all other countries. Institutional rate in the United States is $120/$240; $130/$260 all other countries. Single copies are $10. Special issues are $10. Address all subscription communications to:

THE WESTERN JOURNAL OF MEDICINE 221 Main St., San Francisco, CA 94120-7690 • Tel: (415) 882-5177

Allow six weeks for subscriptions to begin. Past issues must be bought individually. So long as reserve stocks are available, missing issue requests from subscribers are honored for up to six months after the issue date. Thereafter, the single copy rate of $10 is applicable for each issue available. Special issues are $10.

Change of Address—Requests for change of address should give both the old and new address. Allow six weeks for changeover.

SUBMITTING MANUSCRIPTS

Manuscripts for consideration should be sent to the editorial manager, C. Nancarrow, The Western Journal of Medicine, 221 Main St., San Francisco, CA 94120-7690.

"Instructions for Authors"—A complete guide to manuscript submission and *WJM* style available from the publisher. Manuscripts may be prepared in accordance with the "Uniform Requirements for Manuscripts Submitted to Biomedical Journals."

PUBLISHER

Copyright © 1998 by the British Medical Journal Publishing Group • Owned and Published by BMJ Publishing Group and UCSF Stanford Healthcare
All material subject to this copyright appearing in THE WESTERN JOURNAL OF MEDICINE may be photocopied for the noncommercial purpose of scientific or educational advancement. Volumes begin with January and July.

THE WESTERN JOURNAL OF MEDICINE (ISSN 0093-0415/USPS 084 480) is published monthly by BMJ Publishing Inc, 221 Main St., San Francisco, CA 94120-7690. Periodicals postage paid at Easton, Pennsylvania.
POSTMASTER: Send address changes to *The Western Journal of Medicine*, 221 Main Street, San Francisco, CA 94120-7690.

The Western Journal of Medicine

VOLUME 170 • NUMBER 1 • JANUARY 1999

CONTENTS

EDITORIAL

9 **On Being Editor**

LINDA HAWES CLEVER, MD

ARTICLES

11 **Simultaneous Pancreas-Kidney Transplantation: An Overview of Indications, Complications, and Outcomes**

CHRIS E. FREISE, MD; SHUNJI NARUMI, MD; PETER G. STOCK, MD, PhD; and JULIET S. MELZER, MD

From the Department of Surgery, Transplant Division, University of California, San Francisco; and the Department of Surgery, Hirosaki University School of Medicine, Aomori, Japan.

19 **Research Interests of Physicians in Two Practice-Based Primary Care Research Networks**

MARY S. CROUGHAN-MINIHANE, PhD; DAVID H. THOM, MD, PhD; and DIANA B. PETITTI, MD, MPH

From the Department of Family and Community Medicine, University of California, San Francisco; and the Department of Medicine, Division of Family Medicine, Stanford University, Palo Alto, California.

25 **Relationship Between Earlier and Later Mammography Screening—California Medicare, 1992 Through 1994**

JENNIFER D. PARKER, PhD; FABIO SABOGAL, PHD; and TEBEB GEBRETSADIK, MPH

From the California Medical Review, Inc, San Francisco and the National Center for Health Statistics, Hyattsville, Maryland.

28 **Mental Illness in Elementary-School-Aged Children**

ANAND CHABRA, MD, MPH; GILBERTO F. CHÁVEZ, MD, MPH; and EMILY S. HARRIS, MD

From the California Department of Health Services, Maternal and Child Health Branch, Sacramento, California; the Pregnancy and Infant Health Branch, Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia; and the Division of Child, Adolescent and Family Psychiatry, Department of Psychiatry, University of California at Davis, Sacramento, California.

35 **Internal Medical Residents' Ability to Diagnose and Characterize Major Depression**

MITCHELL A. MEDOW, MD, PhD; STEVEN J. BOROWSKY, MD, MPH; SIGNE DYSKEN, MD; STEVE D. HILLSON, MD, MPH; SHARON WOODS, MD; and TIMOTHY J. WILT, MD, MPH

From the Department of General Internal Medicine, the Center for Chronic Disease Outcomes Research, and the Department of Psychiatry, Minneapolis Veterans Affairs Medical Center, Minneapolis, Minnesota and the Department of Internal Medicine, Hennepin County Medical Center, Minneapolis, Minnesota.

41 **Nonsurgical Causes of Pneumoperitoneum**

RICHARD A. MULARSKI, MD; MICHAEL L. CICCOLO, MD; and WILLIAM D. RAPPAPORT, MD

From the University of Arizona College of Medicine and the Department of Surgery, University of Arizona Health Sciences Center, Tucson, Arizona.

ALERTS, NOTICES, AND CASE REPORTS

47 **Cocaine-Induced Intestinal Ischemia**

MUHAMMAD A. WATTOO, MD, and OLUSOLA OSUNDEKO, MD

From the Department of Internal Medicine, University of Pennsylvania Health System, Presbyterian Medical Center, Philadelphia, Pennsylvania.

49 **Potentiation of Warfarin Sodium by Amiodarone-Induced Thyrotoxicosis**

KENNETH A. WOEBER, MD, FRCPE, and IRVING WARNER, MD

From the Department of Medicine, University of California, San Francisco (UCSF)/Mount Zion Medical Center, San Francisco, California.

51 **Persistent Hiccups Induced by Dexamethasone**

JAMES ROSS, BA; MOHSEN ELEDRISI, MD; and PAUL CASNER, MD, PhD

From the Department of Internal Medicine, Texas Tech University Health Science Center, El Paso, Texas.

LESSONS FROM THE PRACTICE

53 **Alone**

WILLIAM E. BYRD, MD

In private practice at Roanoke Valley Internal Medicine and Rheumatology, Roanoke Rapids, North Carolina.

55 **Saying No**

VICTORIA MAIZES, MD

From the Program in Integrative Medicine, The University of Arizona Health Sciences Center, Tucson, Arizona.

OTHER FEATURES

4 **Continuing Medical Education Activities**

57 **Poetry**

58 **Classified Advertising**

60 **Instructions for Authors**

★ Official Journal of the Alaska State Medical Association, the Arizona Medical Association, the California Medical Association, the Denver Medical Society, the Idaho Medical Association, the Nevada State Medical Association, the New Mexico Medical Society, the Utah Medical Association, the Washington State Medical Association, and the Wyoming Medical Society.

Continuing Medical Education

ARIZONA • CALIFORNIA, HAWAII, NEVADA • COLORADO • IDAHO • NEW MEXICO • UTAH • WASHINGTON • WYOMING

ARIZONA

The following list of continuing medical education programs in Arizona is compiled by the Arizona Medical Association. All courses listed have been certified as meeting the criteria for Category I of the ArMA CME Certificate and the AMA Physicians Recognition Award. To list Category I continuing medical education programs, please send information to Arizona Medical Association, 810 West Bethany Home Road, Phoenix, AZ 85013; or phone (602) 246-8901.

Brochures and registration forms are available from the contact person or organization sponsoring the program.

February 7–11, 1999—**International Congress XII on Endovascular Interventions.** Contact: Erika Scott (602) 266-2200 or fax (602) 265-8885. www.endovascularcongress.org

February 26–28, 1999—**Coronary Heart Disease Update.** Hilton Tapatio Cliffs, Phoenix, AZ. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569 (800)421-3756 FAX (303)798-5731.

October 29–31, 1999—**Neurology for the Non-neurologist.** The Phoenician, Scottsdale, AZ. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569 (800)421-3756 FAX (303)798-5731.

December 10–12, 1999—**Managing Respiratory Disease.** The Phoenician, Scottsdale, AZ. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569 (800)421-3756 FAX (303)798-5731.

CONTACT INFORMATION

ArMA—Contact: Arizona Medical Association, 810 W Bethany Home Rd, Phoenix, AZ 85013. (602) 246-8901.

Mayo Clinic-Scottsdale—Contact: Postgraduate Courses, Mayo Clinic-Scottsdale, (602) 301-7447.

U of A—Contact: University of Arizona College of Medicine, Arizona Health Sciences Center, Tucson, AZ 85724. (520) 626-7832; (800) 328-5868.

CALIFORNIA, HAWAII, AND NEVADA

This listing of continuing education programs in California, Hawaii, and Nevada is supplied by the Committee on Continuing Medical Education of the California Medical Association. All courses and meetings listed have been approved for Category I credit toward the CMA Certificate in Continuing Medical Education. To have accredited courses listed here, please send information at least two months in advance to Paulette Richardson, Continuing Medical Education, California Medical Association, PO Box 7690, San Francisco 94120-7690; or phone (415) 882-3387. For more information on accreditation or certification, please write to the above address.

ANESTHESIOLOGY

November 5–7, 1999—**11th Annual Anesthesiology Update.** Monterey Plaza, Monterey, California. Fri–Sat. Contact (916) 734-5390.

CARDIOLOGY

January 18–22, 1999—**The 30th Annual Cardiovascular Conference at Snowmass.** Sponsored by the American College of Cardiology. To be held at Snowmass Conference Center, Snowmass, CO. 23 CME credits. Contact: Registration Secretary, Extramural Programs Dept., American College of Cardiology, 9111 Old Georgetown Rd., Bethesda, MD 20814-1699. Phone (800) 253-4636, ext.695 or Fax (301) 897-9745.

January 29–31, 1999—**Clinical Nuclear Cardiology: Case Review With the Experts. Cardiology Update 1998.** American College of Cardiology at Los Angeles. Thurs.–Sat. Contact: ACC Extramural Programs (800) 253-4636.

February 18–20, 1999—**19th Annual Pathophysiology & Techniques of Cardiopulmonary Bypass.** San Diego Marriott Hotel & Marina. Sponsored by the Cardiothoracic Research &Education Forum. Contact: Aligned Management Associates, Inc. P.O. Box 23220, San Diego CA 92193 (619) 541-1444 or fax (619) 541-1447. www.amainc.com

Coronary Heart Disease Update—March 24–26, 1999–Maui, HI; July 30–August 1, 1999–Yosemite, CA; November 19–21,1999–Las Vegas, NV. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569 (800)421-3756 FAX (303)798-5731.

DERMATOLOGY

January 14–17, 1999—**Practical Dermatology for the Primary Care Physician, San Diego, CA.** Sponsored by Continuing Medical Education Associates. To be held at the Hyatt Regency, La Jolla, San Diego, CA. Method: AV, L, SB, W. Thurs–Sun. 20 hrs credit: AMA, AOA, AAFP. $575. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

March 4–7, 1999—**Practical Dermatology for the Primary Care Physician, Orlando, FL.** Sponsored by Continuing Medical Education Associates. To be held at the Buena Vista Palace at Walt Disney World Village, Orlando, FL. Method: AV, L, SB, W. Thus–Sun. 20 hrs credit: AMA, AOA, AAFP. $575. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

May 23–26, 1999—**Practical Dermatology for the Primary Care Physician, Las Vegas, NV.** Sponsored by Continuing Medical Education Associates. To be held at the Caesars Palace, Las Vegas, NV. Method: AV, L, SB, W. Sun–Wed. 20 hrs credit: AMA, AOA, AAFP. $575. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

Dermatology for the Non-Dermatologist—March 12–14, 1999–Las Vegas, NV; April 23–25, 1999–San Francisco, CA; June 25–27, 1999–Anaheim, CA; September 24–26, 1999–Las Vegas, NV. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569 (800)421-3756 FAX (303)798-5731.

EMERGENCY MEDICINE

February 7–12, 1999—**Emergency Medicine: 22nd Annual UCD Winter Conference.** UC Davis at Hyatt Regency Lake Tahoe, Incline Village, NV. Sun–Fri. 24 hrs. $445. Contact: UCD (916) 734-5390.

March 1–2, 1999—**Improving Emergency Department Patient Satisfaction and Reducing Length of Stay.** Las Vegas, Nevada at Harrah's. Contact: CEME, 5330 Primrose Drive, Suite 250, Fair Oaks, CA 95628. (800) 651-2363.

March 1–5, 1999—**Critical Care, Trauma and Emergency Medicine, 37th Annual Symposium.** Sponsored by the University of Southern California School of Medicine, Postgraduate Division. Caesars Palace Hotel, Las Vegas, NV. 27 hrs. Contact Associate Dean, USC Postgraduate Medicine, 1975 Zonal Ave., KAM 307, Los Angeles, CA 90033. (323) 442-2555 or (800) USC-1119 or FAX (323) 442-2152.

April 12–13, 1999—**High Risk Emergency Medicine.** Las Vegas, Nevada at Harrah's. Contact: CEME, 5330 Primrose Drive, Suite 250, Fair Oaks, CA 95628. (800) 651-2363.

May 6–7, 1999—**Challenges in Pediatric Emergency Medicine.** Las Vegas, Nevada at Harrah's. Contact: CEME, 5330 Primrose Drive, Suite 250, Fair Oaks, CA 95628. (800) 651-2363.

May 13–16, 1999—**Outdoor Emergency Medicine, Scottsdale, AZ.** Sponsored by Continuing Medical Education Associates. To be held at the Marriott Camelback Inn, Scottsdale, AZ. Method: AV, L, SB, W. Thurs–Sun. 32 hrs credit: AMA, AOA, AAFP. $750. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

May 20–21, 1999—**High Risk Emergency Medicine.** Las Vegas, Nevada at Harrah's. Contact: CEME, 5330 Primrose Drive, Suite 250, Fair Oaks, CA 95628. (800) 651-2363.

June 3–4, 1999—**Improving Emergency Department Patient Satisfaction and Reducing Length of Stay.** Chicago, IL at the Holiday Inn Chicago City Centre. Contact: CEME, 5330 Primrose Drive, Suite 250, Fair Oaks, CA 95628. (800) 651-2363.

ENDOCRINOLOGY

January 23, 1999—**NewEra in Diabetes Management.** Cypress Foundation at Doubletree Hotel at Fisherman's Wharf, Monterey. Sat. 7 hrs. $105–$125. Contact: The Cypress Foundation (831) 455-1008 or FAX (831) 455-1060.

March 5, 1999—**Diabetes Update: 1999.** UC Davis at Doubletree Hotel, Sacramento, CA. Friday. 7 hrs. $130. Contact: UCD (916) 734-5390.

March 11–13, 1999—**The Fourth International Conference on Continuous Renal Replacement Therapies.** Hotel del Coronado in San Diego, California. Contact: Shirley Kolkey, Complete Conference Management, 1660 Hotel Circle North, #220, San Diego, CA 92108. (619) 299-6673 or fax (619) 299-6675.

October 22–24, 1999—**Clinical Endocrinology for Primary Care Physicians.** Tropicana, Las Vegas, NV. CME 11 hrs Category 1. Contact: Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569 (800)421-3756 FAX (303)798-5731.

ETHICS

March 3, 1999— **Ethical Problems of Daily Practice.** UC Davis at Cancer Center Auditorium, Sacramento. Wed. 6.5 hrs. Contact: UCD (916) 734-5390.

FAMILY PRACTICE/PRIMARY CARE

January 14–17, 1999—**Practical Dermatology for the Primary Care Physician.** Continuing Medical Education Associates at Hyatt Regency, SF. Thurs.–Sun. 20 hrs. $575. Contact: Victoria Gonzales, PO Box 270469, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

January 14–17, 1999—**Office Orthopedics and Bone Radiology for the Primary Care Physician.** Continuing Medical Education Associates at Hyatt Regency, SF. Thurs.–Sun. 20 hrs. $575. Contact: Victoria Gonzales, PO Box 270469, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

February 11–14, 1999—**Office Gynecology and Women's Health for the Primary Care Physician.** Continuing Medical Education Associates at Hyatt Islandia, San Diego. Thurs.–Sun. 20 hrs. $575. Contact: Victoria Gonzales, PO Box 270469, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

February 12–14, 1999—**California Academy of Family Physicians (CAFP) 51 st Annual Scientific Assembly.** San Diego Concourse, San Diego, CA. 40 hrs. Contact: Clark Franklin, CAFP, 114 Sansome Street, Suite 1305, San Francisco, CA 94104-3824. (415) 394-9121 or fax (415) 394-9119.

February 17–19, 1999—**Annual Review in Family Medicine: Controversies and Challenges in Primary Care.** UCSF at Cathedral Hill Hotel, SF. Wed.–Fri. 16 hrs. $400. Contact: UCSF Program Coordinator, Dept. of Family and Community Medicine (415) 476-5250.

February 27–March 2, 1999—**16th Annual OB/GYN Conference.** OCD at Harrahs Tahoe, South Lake Tahoe, NV. Sat.–Tues. 16 hrs. $325. Contact: UCD (916) 734-5390.

March 27, 1999—**Primary Care Gastroenterology.** UC Davis at Cancer Center Auditorium, Sacramento, CA. Saturday. Contact: UCD (916) 734-5390.

April 10, 1999—**Primary Care Orthopedics, Lower Extremities.** UC Davis at Holiday Inn Northeast, Sacramento, CA. Sat. Contact: UCD (916) 734-5390.

April 17, 1999—**Primary Care Cardiology.** UC Davis at Cancer Center Auditorium, Sacramento, CA. Sat. Contact: UCD (916) 734-5390.

KEY TO ABBREVIATIONS

DREW:	Charles R. Drew Postgraduate Medical School, Office of Continuing Medical Education, (213) 563-4800.
LLU:	Loma Linda University, Continuing Medical Education Programs, (909) 824-4963.
STAN:	Stanford University, Postgraduate Education, (415) 723-5594.
UCD:	University of California, Davis, Office of Continuing Medical Education, (916) 734-5390.
UCI:	University of California, Irvine, Memorial/UCI Center for Health Education, (714) 824-5926.
UCLA:	University of California, Los Angeles, Continuing Education in Medicine and Health Sciences, (310) 794-2620.
UCSD:	University of California, San Diego, Office of Continuing Medical Education, (619) 534-3940.
UCSF:	University of California, San Francisco, Extended Programs in Medical Education, (415) 476-4251.
USC:	University of Southern California, Postgraduate Division, (800) USC-1119.

April 28, 1999—**Mangement of Benign Uterine Conditions.** UC Davis at Cancer Center Auditorium, Sacramento, CA. Wed. 4 hrs. $50. Contact: UCD (916) 734-5390.

May 14–18, 1999—**Primary Care Essentials, San Francisco, CA.** Sponsored by Continuing Medical Education Associates. To be held at the Grand Hyatt on Union Square, San Francisco, CA. Method: AV, L, SB, W. Thurs–Sun. 32 hrs credit: AMA, AOA, AAFP. $750. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

INFECTIOUS DISEASE

February 5–6, 1999—**Infectious Disease Update: 1999.** UC Davis at Hilton Hotel, Sacramento. Fri–Sat. Contact: UCD (916) 734-5390.

February 11–13, 1999—**Epidemiology and Prevention of Infectious Diseases: Emerging Infectious Diseases.** UCSF at Crowne Plaza, Union Square, San Francisco. Thurs–Sat. 14.5 hrs. $470. Contact: UCSF (415) 476-5808.

February 21–26, 1999—**Winter Course in Infectious Diseases, Snowmass, Colorado-25th Anniversary Meeting.** Sponsored by the Division of Infectious Diseases and Geographic Medicine, Stanford University School of Medicine and Research Institute, Palo Alto Medical Foundation. 28 hrs. $75–$350. Contact: Trisha Mitchell, Meeting Coordinator (800) 535-7814 or fax (215) 422-1283.

INTERNAL MEDICINE

March 19–25, 1999—**Internal Medicine, San Diego CA.** Sponsored by Continuing Medical Education Associates. To be held at the Hotel del Coronado, San Diego, CA. Method: AV, L, SB, W. Fri–Thurs. 45 hrs credit: AMA, AOA, AAFP. $895. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

August 22–27, 1999—**New Advances in Internal Medicine.** Embassy Suites, Monterey, CA. Sun–Fri. Contact (916) 734-5390.

NEPHROLOGY

February 4–6, 1999—**Advanced Nephrology: Nephrology for the Consultant.** Sponsored by UC San Diego. To be held at the Coronado Island Marriott Resort, Coronado, CA. 17 hrs credit:AMA. $175, $425. Contact: Shirley Kolkey, 1660 Hotel Circle North, #220, San Diego, CA 92108. Phone (619) 299-6673 or Fax (619) 299-6675; e-mail c-c-m@worldnet.att.net

NEUROLOGY

February 10–12, 1999—**Recent Advances in Neurology.** UCSF at Mark Hopkins Inter-Continental Hotel, San Francisco. Wed–Fri. 15 hrs. $425. Contact: UCSF (415) 476-0318.

May 14–16, 1999—**Neurology for the Non-neurologist.** Bally's, Las Vegas, NV. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569 (800)421-3756 FAX (303)798-5731.

OB/GYN

February 11–14, 1999—**Office Gynecology and Women's Health for the Primary Care Physician, San Diego, CA.** Sponsored by Continuing Medical Education Associates. To be held at the Hyatt Islandia, San Diego, CA. Method: AV, L, SB, W. Thurs–Sun. 20 hrs credit: AMA, AOA, AAFP. $575. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

February 25–28, 1999—**Office Gynecology and Women's Health for the Primary Care Physician, Orlando, FL.** Sponsored by Continuing Medical Education Associates. To be held at the Buena Vista Palace at Walt Disney World Village, Orlando, FL. Method: AV, L, SB, W. Thurs–Sun. 20 hrs credit: AMA, AOA, AAFP. $575. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

February 27–March 2, 1999—**16th Annual OB/GYN Conference.** OCD at Harrahs Tahoe, South Lake Tahoe, NV. Sat.–Tues. 16 hrs. $325. Contact: UCD (916) 734-5390.

April 28, 1999—**Mangement of Benign Uterine Conditions.** UC Davis at Cancer Center Auditorium, Sacramento, CA. Wed. 4 hrs. $50. Contact: UCD (916) 734-5390.

September 25–26, 1999—**Ultrasound Update: 1999.** Hilton Hotel, Sacramento, CA. Sat.–Sun. (916) 734-5390.

December 10–12,1999—**Issues in Women's Health.** Tropicana, Las Vegas, NV. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569 (800)421-3756 FAX (303)798-5731.

ORTHOPEDICS

January 14–17, 1999—**Office Orthopedics and Bone Radiology for the Primary Care Physician, San Diego, CA.** Sponsored by Continuing Medical Education Associates. To be held at the Hyatt Regency, La Jolla, San Diego, CA. Method: AV, L, SB, W. Thurs–Sun. 20 hrs credit: AMA, AOA, AAFP. $575. Contact: CMEA Monica L. Lier. (800) 993-2632 or (619) 674-5200.

February 25–28, 1999—**Office Orthopedics and Bone Radiology for the Primary Care Physician, New Orleans, LA.** Sponsored by Continuing Medical Education Associates. To be held at the Royal Sonesta Hotel, New Orleans, LA. Method: AV, L, SB, W. Thurs–Sun. 20 hrs credit: AMA, AOA, AAFP. $575. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

February 25–28, 1999—**Office Orthopedics and Bone Radiology for the Primary Care Physician, Las Vegas, NV.** Sponsored by Continuing Medical Education Associates. To be held at the Caesars Palace, Las Vegas, NV. Method: AV, L, SB, W. Sun–Wed. 20 hrs credit: AMA, AOA, AAFP. $575. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

June 13–18, 1999—**23rd Annual Fingers to the Toes Primary Care Orthopaedics.** To be held at the Stanford Sierra Camp, near South Lake Tahoe, Fallen Leaf Lake, CA. Sun–Fri. Contact (916) 734-5390.

PEDIATRICS

January 29–31,1999—**37TH Clinical Conference Pediatric Anesthesiology.** Disneyland Hotel, 1150 W. Cerritos Avenue, Anaheim, CA 92802. Sponsored by The Pediatric Anesthesiology Foudation. $250-$295. Contact David J Steward, M.B., Program Director, Pediatric Anesthesiology Conference Box #3, Childrens Hospital Los Angeles, P.O. Box 54700, Los Angeles, CA 90054. Phone (213) 669-2262 or Fax (213) 660-8983.

February 14–17, 1999—**Pediatrics Update 1999, San Diego, CA.** Sponsored by Continuing Medical Education Associates. To be held at the Hyatt Islandia, San Diego, CA. Method: AV, L, SB, W. Sun–Wed. 20 hrs credit:AMA, AOA, AAFP. $575. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

February 28–March 3, 1999—**Pediatrics Update 1999, Orlando, FL.** Sponsored by Continuing Medical Education Associates. To be held at the Buena Vista Palace at Walt Disney World Village, Orlando, FL. Method: AV, L, SB, W. Sun–Wed. 20 hrs credit:AMA, AOA, AAFP. $575. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

March 19–20, 1999—**Pediatrics Update: 1999.** UC Davis at Cancer Center Auditorium, Sacramento, CA. Fri–Sat. Contact: UCD (916) 734-5390.

May 6–8, 1999—**Advances and Controversies in Clinical Pediatrics.** UCSF at Ritz-Carlton Hotel on Nob Hill, SF. Contact: UCSF (415) 476-5808 or FAX (415) 502-1795.

July 16–17,1999—**Seventh Annual Pediatric Update.** Sponsored by Lucile Packard Children's Health Services at Stanford and faculty from UCSF and Stanford Schools of Medicine. Lucile Packard Children's Hospital. Contact: Elinor Meyer, Continuing Medical Education and Physician Relations Department, Lucile Packard Children's Hospital, 725 Welch Road, Palo Alto,CA 94304 (650) 497-8554.

PLASTIC SURGERY

March 18–20, 1999—**11th Annual Symposium on Aesthetic Surgery.** UCSF at Palace Hotel, San Francisco. Thurs–Sat. 19.5 hrs. $950. Contact UCSF (415) 476-5808.

PRIMARY CARE

February 26–28, 1999—**Management of the HIV-Infected Patient–A Practical Approach for the Primary Care Practitioner.** Le Meridien, New Orleans, LA. Contact: Center for Bio-Medical Communication, Inc. (201) 342-5300 or FAX (201) 342-7555; email cmeinfo@cbcbiomed.com

March 27, 1999—**Primary Care Gastroenterology.** UCDMC, Cancer Center Auditorium, Sacramento, CA. Sat. (916) 734-5390.

April 10, 1999—**Primary Care Orthopedics, Lower Extremities.** Holiday Inn Northeast, Sacramento, CA. Sat. (916) 734-5390.

April 17, 1999—**Primary Care Cardiology.** UCDMC, Cancer Center Auditorium, Sacramento, CA. Sat. (916) 734-5390.

June 5–7, 1999—**8th Annual Primary Care Treatment of Pain.** Tenaya Lodge at Yosemite, Fish Camp, CA. Sat–Mon. (916) 734-5390.

July 25–29, 1999—**19th Annual Current Concepts in Primary Care Cardiology.** Granlibakken Conference Center, Tahoe City, CA. Sun–Thurs. (916) 734-5390.

October 22–24, 1999. **Clinical Endocrinology for Primary Care Physicians.** Tropicana, Las Vegas, NV. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569 (800)421-3756 FAX (303)798-5731.

PSYCHIATRY

January 24–29, 1999—**Annnual Midwinter Program for Psychiatrists.** UC Davis at Hyatt Regency Incline Village, NV. Sun–Fri. 25 hrs. $495.

April 10, 1999—**Psychiatry Update.** UC Davis at Cancer Center Auditorium, Sacramento, CA. Sat. Contact: UCD (916) 734-5390.

RADIOLOGY

February 25–28, 1999—**Up to Date Radiology in the Desert.** Mira Monte Resort, Indian Wells, California. Credit 26 hrs. AMA. $495-$750. Contact: Ryals & Associates, Inc., PO Box 1925, Roswell, GA, 30077-1925; (770)641-9773; fax (770)552-9859; email: webmaster@ryalsmeet.com.

RESPIRATORY

March 19–20, 1999—**Cystic Fibrosis Caregivers Symposium.** UC Davis at Marriott Hotel, Napa, CA. Fri–Sat. Contact: UCD (916) 734-5390.

Managing Respiratory Disease–April 23–25, 1999–Las Vegas, NV; June 11–13, 1999–San Francisco, CA; August 6–8, 1999–Monterey, CA. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569 (800)421-3756 FAX (303)798-5731.

SURGERY

January 15–16, 1999—**What's New General Surgery.** UC Davis at Hyatt Regency Sacramento at Capitol Park. Fri–Sat. 13 hrs. $280. Contact: UCD (916) 734-5390.

April 24, 1999—**3rd Annual Organ Transplant Conference.** UCD at Cancer Center Auditorium, Sacramento, CA. Sat. Contact UCD (916) 734-5390.

GENERAL/MULTIDISCIPLINARY

January 29–31, 1999—**Research Study Club, 65th Clinical Conference.** To be held at the Universal City Hilton & Towers, CA. 15 hrs credit. $190–$400. Contact: Mrs.Ball (909) 677-4482 or fax (909) 677-7904; email: lbll@aol.com.

April 28–May 8, 1999—**Blue Water Medical Seminar.** Tri City Medical Center at Baja California aboard Royal Star Sportfisher. Wed–Sun. 20 hrs. $3300. Contact: Ronald Mcdak (760) 727-7863.

May 16–19, 1999—**Alternative Medicine, Scottsdale, AZ.** Sponsored by Continuing Medical Education Associates. To be held at the Mariott Camelback Inn, Scottsdale, AZ. Method: AV, L, SB, W. Sun–Wed. 20 hrs credit: AMA, AOA, AAFP. $575. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

June 22–29, 1999—**Mindfulness-Based Stress Reduction in Mind-Body Medicine.** To be held at the Mana Lae Retreat Center, Maui, Ha. $995. Contact: Steve Flowers (530) 898-1495.

LOSS PREVENTION

September 22–25, 1999—**Legal Issues in Damaged Brain Injury Cases.** Westin St. Francis Hotel, San Francisco, CA. Wed–Sat. Contact (916) 734-5390.

HOME STUDY/SELF ASSESSMENT

California Physicians' Legal Handbook Series. California Medical Association. Contact: CMA, PO Box 7690, San Francisco 94120-7690. (800) 882-1262.

Breast Cancer, Early Detection and Control. Texas Medical Association. **CD ROM.** $70. 2 hrs. Contact: Texas Medical Association (800) 880-1300; http://www.texmed.org/health_science/hs_poep.html

COLORADO

This listing of continuing medical education programs in Colorado is compiled by the Denver Medical Society. To list CME programs here, please send information at least two months in advance to: Mr Robert L. Kennedy, Denver Medical Society, 1850 Williams Street, Denver, CO 80218; or telephone (303) 377-1850.

Brochures, course information, and registration forms are available from the contact person or organization.

Tuesday Noon Conferences—**Various Topics in Medicine.** Lutheran Medical Center, Wheat Ridge. Contact: Jean A. Kline, (303) 425-2951.

First Wednesday of Each Month—**Various Topics in Neurology.** Colorado Society of Clinical Neurologists. Contact: Colorado Society of Neurologists, (303) 449-3566.

Second Wednesday of Each Month—**Cardiovascular Education Series.** St Anthony Hospital at St Anthony Hospital, Denver. Contact: Rose Powell, (303) 629-3678.

February 4–6, 1999—**Neurology For The Non-Neurologist.** Hyatt Regency, Cancun Mexico. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

February 5–7, 1999—**Arrhythmias: Interptretation, Diagnosis & Management** MGM Grand, Las Vegas, NV Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

February 12–14, 1999—**Clinical Endocrinology For Primary Care Physicans.** Beaver Run Resort, Breckenridge, CO.Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

February 19–21, 1999—**Managing Respiratory Diseases.** Marriot's Casa Marina, Key West, FL. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

February 25–27, 1999—**Dermatology For The Non-Dermatologist.** Atlantis Paradise Resort, Bahamas. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

February 26–28, 1999—**Coronary Heart Disease Update.** Hilton Tapatio Cliffs, Scottsdale, AZ. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

March 12–14, 1999—**Dermatology For The Non-Dermatologist.**Riviera Hotel & Casino, Las Vegas, NV. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

March 25–27, 1999—**Neurology For The Non-Neurologist.** Grand Beach Resort, St. Thomas, USVI. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

March 25–27, 1999—**Clinical Endocrinology For Primary Care Physicans.** Marriott's Beach Resort, St. Grand Cayman. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

March 26–28, 1999—**Managing Respiratory Diseases.** Buena Vista Palace,Orlando,FL. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

April 8–10, 1999—**Coronary Heart Disease Update.** Hyatt Regency, Aruba Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

April 8–10, 1999—**Clinical Endocrinology For Primary Care Physicans.** The Westin Resort, St John, USVI. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

April 9–11, 1999—**Arrhythmias: Interptretation, Diagnosis &Management** Hilton Tapatio Cliffs, Scottsdale, AZ. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

April 9–11, 1999—**Neurology For The Non-Neurologist.** Marriott's Casa Marina, Key West, FL. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

April 23–25,1999—**Managing Respiratory Diseases.** Bally's, Las Vegas, NV. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

April 23–25,1999—**Dermatology For The Non-Dermatologist.** Parc Fifty-five, San Francisco, CA. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

April 30–May 2, 1999—**Dermatology For The Non-Dermatologist.** South Sea Plantation, Captiva Island, FL. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

April 30–May 2, **Clinical Endocrinology For Primary Care Physicans.** Hyatt Regency, New Orleans, LA. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

May 14–16, 1999—**Managing Respiratory Diseases.** Hilton Resort, Hilton Head, SC. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

May 14–16, 1999—**Neurology For The Non-Neurologist.** Bally's, Las Vegas, NV. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

CONTACT INFORMATION

U of Colo—Contact: University of Colorado Health Sciences Center, School of Medicine, Office of Continuing Medical Education, 4200 E 9th Ave, Denver 80262. (303) 372-9050 or (800) 882-9153; FAX (303) 372-9065.

IDAHO

The listing of continuing medical education programs in Idaho is compiled by the Ada County Medical Society. To list CME programs here, please send information at least two months in advance to: Ada County Medical Society, Inc. 305 W. Jefferson, PO Box 2668, Boise, Idaho 83701. (208) 336-2930.

Brochures, course information, and registration forms are available from the contact person or organization.

February 19–21, 1999—**ACMS 40th Annual Medical Winter Clinics.** McCall, Idaho, Shore Lodge Inn. 11.5 hrs. Contact: Judy Barningham (208) 336-2930 or Marie Chester (208) 331-1478.

NEW MEXICO

Information, requests for accreditation, and items to be listed should be sent to the chair of the CME Committee, New Mexico Medical Society, 7770 Jefferson, Suite 400, Albuquerque, NM 87109, at least two months in advance. For information on CME accreditation or on the CME requirements of the New Mexico Board of Medical Examiners, please write to the above address or call (505) 828-0237.

NOTE: Course information in the following listing is subject to change on occasion. Check with the sponsoring institution for current details.

Every First and Third Tuesday—**Building and Implementing Clinical Practice Guidelines at the Point of Care.** Contact: Thomas A. Naegele, DO, (505) 275-7267.

April 28–30, 1999—**The Fourth Annual Clinical Cardiology Management and Diagnostic Dilemmas.** Eldorado Hotel, Santa Fe, NM. 17 Category 1 AMA. Contact: Registration Secretary, American College of Cardiology, 9111 Old Georgetown Rd, Bethesda, MD 20814-1699 (800) 253-4636, ext.695.

July 30–August 1, 1999–**Neurology for the Non-neurologist.** Eldorado Hotel, Sante Fe, NM. CME 11 hrs Category 1. Contact: Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569 (800)421-3756 FAX (303)798-5731.

SATELLITE COURSES

Contact: Joe Treat or Jim Cato, Immunization Program, (505) 827-2366.

CONTACT INFORMATION

UNM SOM—University of New Mexico School of Medicine, Office of CME, PO Box 713, Albuquerque 87131, (505) 277-3942.

UTAH

This listing of continuing medical education courses in Utah is compiled and edited by the CME office of the Utah Medical Association. All courses listed have been certified by CME accredited institutions as meeting the criteria for Category 1 of the Physician's Recognition Award of the American Medical Association. Accredited institutions wishing to list AMA Category 1 CME courses here should send information at least two months in advance to the Office of Continuing Medical Education, 540 East Fifth South, Salt Lake City, UT 84102; or phone (801) 355-7477. For information on CME accreditation, please write the CME office at the above address.

NOTE: Course information in the following listing is subject to change on occasion. Check with the sponsoring institution.

January 6–10, 1999—**MRI at Snowbird.** Cliff Lodge, Snowbird, Utah. Credit 20 hrs. AMA. $400-$650. Contact: Ryals & Associates, Inc., PO Box 1925, Roswell, GA, 30077-1925; (770)641-9773 or fax (770)552-9859; email: webmaster@ryalsmeet.com. www.ryalsmeet.com

MEDICAL GRAND ROUNDS

Weekly—**Grand Rounds in Internal Medicine, Psychiatry, OB/GYN, and Pediatrics.** Contact: UUSM.

Weekly—**Pediatric Grand Rounds.** Contact: PCMC.

WASHINGTON

The listing of continuing medical education programs in Washington state is compiled by the Washington State Medical Association. To list Category 1 programs here, please send information at least two months in advance to Continuing Medical Education, Washington State Medical Association, 2033 Sixth Avenue, Suite 1100, Seattle, WA 98121; or phone (206) 441-9762 or (800) 552-0612.

Brochures and registration forms are available from the contact person or organization listed at the end of each course or in the list of course sponsors and contact information.

COURSE SPONSORS AND CONTACT INFORMATION

CME HARBORVIEW—Contact: Gayle Splater, Cytology Continuing Education, Dept. of Pathology, Harborview Medical Center, 325 Ninth Ave, Seattle, WA 98104, (206) 223-5953.

PCMS CME—Contact: Executive Director, College of Medical Education, 705 S Ninth, No. 203, Tacoma, WA 98405, (206) 627-7137.

U/W (UNIVERSITY OF WASHINGTON)—Contact: U/W School of Medicine, Div. of CME, SC-50, Seattle, WA 98195, (206) 543-1050.

VMMC (VIRGINIA MASON MEDICAL CENTER)—Contact: Linda Orgel, Division of Continuing Medical Education, Virginia Mason Medical Center, PO Box 900, Seattle, WA 98111, (206) 340-2058.

WSMA—Washington State Medical Association, Continuing Medical Education, 2033 Sixth Ave, Ste 1100, Seattle, WA 98121, (206) 441-9762.

OTHER CME OPPORTUNITIES

Brochures and registration forms are available from the contact person or organization listed at the end of each course or in the list of course sponsors and contact information.

Annual Meeting and Course: International Spine Imaging Symposium. February 15–17, 1999. Registry Resort, Naples, Florida. Credit 19.5 hrs. AMA. $250–$650. Contact: Ryals & Associates, Inc., PO Box 1925, Roswell, GA, 30077-1925; (770)641-9773; fax (770)552-9859; email: webmaster@ryalsmeet.com.

Breast Imaging Today and Tomorrow. January 25–28, 1999. Boca Raton Resort and Club, Boca Raton, Florida. Credit 23 hrs. AMA. $495–$695. Contact: Ryals & Associates, Inc., PO Box 1925, Roswell, GA, 30077-1925; (770)641-9773; fax (770)552-9859; email: webmaster@ryalsmeet.com.

Breast Imaging Today and Tomorrow. February 15–19, 1999. Buena Vista Palace Resort and Spa, Lake Buena Vista, Florida. Credit 23 hrs. AMA. $495–$695. Contact: Ryals & Associates, Inc., PO Box 1925, Roswell, GA, 30077-1925; (770)641-9773; fax (770)552-9859; email: webmaster@ryalsmeet.com.

Musculoskeletal MR. January 18–22, 1999. The Ritz-Carlton Resort Hotel, West Palm Beach, Florida. Credit 22.5 hrs. AMA. $450–$695. Contact: Ryals & Associates, Inc., PO Box 1925, Roswell, GA, 30077-1925; (770)641-9773; fax (770)552-9859; email: webmaster@ryalsmeet.com.

Predoctoral Education Conference. February 4–7, 1999. Savannah Marriott Riverfront, Savannah, Georgia. Contact: Ray Rosetta, Meetings and Programs Director, Society of Teachers of Family Medicine, 8880 Ward Parkway, Kansas City, Missouri 64114. Phone (800) 274-2237, ext. 4512.

STFM Family Conference. March 3–7, 1999. Kiawah Resort, Kiawah Island, South Carolina. Contact: Ray Rosetta, Meetings and Programs Director, Society of Teachers of Family Medicine, 8880 Ward Parkway, Kansas City, Missouri 64114. Phone (800) 274-2237, ext. 4512.

5th Annual Neuroradiology: A Comprehensive Review. February 2–6, 1999. The Ritz-Carlton Resort Hotel, West Palm Beach, Florida. Credit 24 hrs. AMA. $450–$695. Contact: Ryals & Associates, Inc., PO Box 1925, Roswell, GA, 30077-1925; (770)641-9773; fax (770)552-9859; email: webmaster@ryalsmeet.com.

32nd Annual Spring Conference. April 28–May 2, 1999. Sheraton Seattle Hotel & Towers, Seattle, Washington. Contact: Ray Rosetta, Meetings and Programs Director, Society of Teachers of Family Medicine, 8880 Ward Parkway, Kansas City, Missouri 64114. Phone (800) 274-2237, ext. 4512.

35th Annual Forensic Dentistry. March 7–11, 1999. Holiday Inn, Silver Spring, Maryland. Credit 38 hrs. $300–$675. Contact: Ruth Murphy, CAME, Armed Forces Institute of Pathology, Washington, DC 20306-6000; (800) 577-3749 or (202) 782-2637; email: came@afip.osd.mil; www.afip.org.

58th Annual American Occupational Health Conference. April 23–30, 1999. Ernest N. Morial Convention Center, New Orleans, Louisiana. Contact: ACOEM Education Dept., 55 W. Seeger Road, Arlington Heights, IL 60005; (847) 228-6850 or fax (847) 228-1856; www.acoem.org.

80th Annual Session-American College of Physicians-American Society of Internal Medicine. April 22–25, 1999. Ernest N. Morial Convention Center, New Orleans. Credit 29 hrs. Contact: ACp-ASIM Customer Service (800) 523-1546, ext. 2600; www.acponline.org.

NOTICE

State Associations should send their CME listings for publication to:

Catherine Nancarrow, Editorial Manager
The Western Journal of Medicine
221 Main Street
San Francisco, CA 94120-7690

(415) 882-5177 • Fax (415) 882-3379 • rstraube@bmjgroup.com

Editorial

On Being Editor

Mark Twain hated editors. He once said, "Yours was not in the beginning a criminal nature. But circumstances changed it. At age nine, you stole sugar. At age fifteen, you stole money. At age twenty, you stole horses. At age twenty-five, you committed arson. At age thirty, hardened in crime, you became an editor. Since then, your descent has been rapid."[1]

Contemporary writers temper their comments only slightly: "My husband and I are both writers. During dinner conversations, we often tell our children about our working days. It wasn't clear how much they absorbed until one day I overheard my 7-year-old, Lucy, cry out in frustration at her 5-year-old sister, Charlotte, 'You, you . . . you editor!'"[2]

There is another side. It may not excuse editors' style nor assuage authors' outrage, but it explains why some ardently pursue a calling that has provoked criticism across the centuries. The great editor Hugh Clegg cited Voltaire's ringing cry for freedom as one of our guiding principles. "I disapprove of what you say, but I will defend to death your right to say it."[3] Editors grapple with issues that reflect science and society and the quest for freedom coupled with responsibility. We look for accuracy and honesty, aware of attempts at duplicate publication and fraud. We struggle with the definitions and duties of being an author or an editor, relationships with the media and publisher, conflicts of interest beyond simply accepting advertising, and pros and cons of peer review. Given past and present pressures, why would anyone want to be an editor?

Looking back on eight and a half years of being editor of *The Western Journal of Medicine*, and as I pass the baton to others, I ponder several answers. Editors can have the satisfaction of finding paths through thickets of controversy. There is plenty of controversy around issues such as how to preserve patients' privacy while protecting public health.[4] Editors also have the opportunity to lead, and to shape opinion. To do so, however, requires that editors write. My mother was an author. As a child, I watched her struggle with words, words, words, and decided that writing was far too hard a thing to do. I was right, but writing is necessary if one is to use the editor's bully pulpit.

Editors can innovate. We took the opportunity to publish Roger Bulger's book, *The Quest for Mercy: The Forgotten Ingredient in Health Care Reform,* in three parts.[5–7] We have watched it sail well into a second edition. Dr Russell Altman championed our new informatic series. Assistant Editor Margaret Kaufman broke ground as our poetry recruiter and editor, allowing the journal to publish outstanding work in keeping with one of my early assertions: "History, literature, performing arts, fine arts are important to medicine because they are important to patients and to physicians. In their own way, they are as important as technology and technique. It is interesting to explore the relationships between basic and applied sciences and the humanities. DNA is poetry."[8] Editors can preserve. We have continued the distinctive features started by my splendid predecessor, Dr Malcolm S. M. Watts, such as the Epitomes and special issues.

Editors can raise the standards of editing and publishing. *The Western Journal of Medicine* has the good fortune of being part of the International Committee of Medical Journal Editors, also known as the Vancouver Group. Our meetings are marked by yeasty decisions that, twenty years ago, led to recommendations regarding uniform manuscript format and, now, venture into publication policies and ethics. Editors can encourage scientists by simplifying writing requirements and can improve the research enterprise by illuminating issues.

Editors can help journals live. I took on the editorship's honor and responsibilities with a determination to make a difference in the care of patients and to be certain that the journal would be of practical value to practicing physicians. We have carried on with the journal under the threat of extinction not only once but twice, and now celebrate its bright future. Although sometimes it feels lonely to be the only one who is editor, in fact, the editor is not alone. All of the accomplishments have been achieved with the help of others.

The past eight years have been marked by high challenge, high satisfaction, low points, good company, great learning experiences, some touching moments and some funny moments. I alluded to the challenge, satisfaction, and low points above. Good company includes Associate Editors, Drs Lloyd Hollingsworth Smith, Jr and Edward D. Harris, Jr, essential partners. During the hard times, they were joined by other encouragers, negotiators, and/or fund raisers such as Sandra Bressler and the Board of Directors of the San Francisco Medical Society; and Drs Ralph Crawshaw, Virginia Ernster, John Holbrook, Stephen Hulley, Jack Lewin, Helen Ranney, Joseph Silva, Robert Sparks, C. John Tupper and Dwight Wilbur.

Learning experiences were too numerous to count. They include learning how to wheedle, even needle, authors and reviewers as due dates and publication schedules approached inexorably. That is when editors realize the importance of being flexible. I learned how to appeal for special support for special projects and how to comfort disappointed authors and concerned readers and how to correct our mistakes. I tried to learn how to cope with biases. I relearned that expectations rarely come true. For example, I had anticipated and welcomed the opportunity to insert contemplative time into my full-tilt life. I envisioned walking in a cloister, as it were, hands clasped in back, thinking on matters philosophical. That dream vanished like the dew at dawn as the journal entered its times of trouble. Goals remained, however, and we have been able to serve patients and profession.

Touching moments came in Lessons from the Practice, so ably co-edited by Drs Stephen McPhee and Jack Rodnick, and from authors' comments, sometimes in response to reviewers' criticisms, such as, "I apologize for the insensitivity and lack of humility I have shown in this essay . . . Perhaps it was self-hatred. Please tell the reviewers their comments shall not be forgotten." Kudos were warming, too:

- "*The Western Journal of Medicine* has always been one of the few journals that I go through page by page."
- "I read *The Western Journal* first."
- "I always read *The Western Journal of Medicine* even if I'm behind in my reading."

As for funny moments:

- From an author: "I wish to assure you I am not unhappy about rejection. I just hate it. Perhaps you have noticed, I have a way of telegraphing my intense dislike through all available channels. I hate the message not the messenger."
- From a reviewer: "This is a seriously pompous author."
- From a paper: "We report a case of orf in a woman following traumatic contact with a lamb's head." (We were eager to read the rest of the case report. It described an accident while cooking, not wrestling.)
- There was an invitation to attend the first World Congress on the Health Significance of Garlic and Garlic Constituents. There were health tips regarding, for example, the usefulness of wine as treatment for urinary frequency. Finally, one person wrote that a voice spoke to him from the darkness of a dream and said, "The cure for AIDS is the tapeworm. I know this letter may sound strange, but I would hate to have been given the answer to a disease that is the scourge of civilization and not do anything about it."

It has been good to be part of the core of medical editing and publishing. My pantheon is full. I am awed by the prodigious efforts of authors who design, perform, and describe studies that will improve health. My heart quickens at the thought of reviewers who consistently go an extra mile for our profession with far too little recognition. Some write pages of suggestions and check references for accuracy. Readers are both receivers and transmitters; your comments are essential to the journal's improvement. The Associate and Assistant Editors, the Senior Editorial Council, and the Editorial Board provide strength, good advice, and creative suggestions as, might I add, do family, friends, and colleagues. As I said eight and a half years ago, "Medicine is difficult. The life is hard. We need to replenish our energy and soothe our souls."[8] You have done that for me over these years. I hope we have done the same for you. Thank you.

Linda Hawes Clever, MD
Editor

REFERENCES

1. Twain M. Browsing around. Buffalo Express Nov. 27, 1869

2. Weber K. All in a day's work. Reader's Digest 1994; 145:48

3. Clegg H. Some principles and problems of medical editing. Int Rec Med 1960; 173:419

4. Clever LH. Obtain informed consent before publishing information about patients. JAMA 1997; 278:628–629

5. Bulger R. The quest for mercy: the forgotten ingredient in health care reform. West J Med 1997; 167:362–373

6. Bulger R. The quest for mercy: the forgotten ingredient in health care reform. West J Med 1997; 167:443–456

7. Bulger R. The quest for mercy: the forgotten ingredient in health care reform. West J Med 1997; 168:54–72

8. Clever LH. Plus ça change, plus c'est la même chose [Editorial]. West J Med 1990; 153:192

Articles

Simultaneous Pancreas-Kidney Transplantation: An Overview of Indications, Complications, and Outcomes

CHRIS E. FREISE, MD; *San Francisco, California*; SHUNJI NARUMI, MD; *Aomori, Japan*; PETER G. STOCK, MD, PhD; *and* JULIET S. MELZER, MD; *San Francisco, California*

Simultaneous pancreas-kidney transplantation (SPK) has become an accepted therapy for the treatment of patients with insulin-dependent diabetes mellitus and renal failure from diabetic nephropathy. The procedure has evolved over the last twenty years, and refinements in technique, better organ preservation solutions, and more potent immunosuppressive therapies have improved one-year graft-survival rates to 81% for the pancreas and 88% for the kidney (International Pancreas Transplant Registry Data-1996). Proper patient selection is important, given the increased complexity of the procedure, the increased need for immunosuppression, and the need for compliance with postoperative medications and monitoring. The benefits of a successful SPK include more physiologic glucose metabolism and freedom from dialysis. This review will describe the indications and selection process for potential candidates, outline the procedure and postoperative care, and discuss the potential impact on secondary complications of diabetes mellitus. It will then discuss results and complications from the use of current protocols and immunosuppression at the University of California at San Francisco.

(Freise CE, Narumi S, Stock P, Melzer JS. Simultaneous pancreas-kidney transplantation: an overview of indications, complications and outcomes. West J Med 1999; 170:11–18)

Introduction

Diabetes mellitus is prevalent in about five percent of the general population. Complications of diabetes, including retinopathy, microvascular disease, and renal disease, cause significant morbidity and mortality in this group of patients. Diabetes and its complications are the eighth leading cause of death in the United States,[1] the leading cause of renal failure and blindness in adults, and the most frequent, underlying disease leading to amputations.[2]

Approximately 30% of patients with diabetes require daily insulin injections. The administration of insulin in this fashion prevents the serious, metabolic derangements that can occur with hyperglycemia, and tight control of serum glucose may slow or prevent the secondary complications of diabetes.[3] No exogenous insulin administration, however, can compare to the physiologic delivery of insulin by an intact pancreas. For this reason, whole-organ, pancreas transplantation was first attempted in humans in 1966. The development of the surgical techniques for successful transplantation, the use of newer immunosuppressionants, and an understanding of the pitfalls and complications following pancreas transplantation have enabled graft- and patient-survival rates to reach levels far superior to early results. These results justify offering the procedure to carefully selected patients, for whom earlier intervention in the course of the disease will possibly result in better prevention of secondary complications.

The University of California at San Francisco (UCSF) initiated a program of simultaneous pancreas-kidney transplantation (SPK) in 1989. Since that time, over 140 patients have undergone the procedure at our institution. This review will outline our indications and approach to patient selection, describe the surgical procedure and its complications, and comment on current results and effects on secondary complications.

Indications and Patient Selection

Simultaneous pancreas-kidney transplantation is typically offered to patients who have insulin-dependent diabetes mellitus and in whom diabetic nephropathy and renal insufficiency have developed. Many of these potential recipients have other manifestations of diabetes, including retinopathy, neuropathy and gastropathy.

From the Department of Surgery, Transplant Division, University of California, San Francisco (Drs Freise, Stock, and Melzer) and the Department of Surgery, Hirosaki University School of Medicine, Hirosaki City, Aomori, Japan (Dr Narumi).

Reprint requests to Chris E. Freise, University of California, San Francisco, Box 0780, Room M896, 505 Parnassus Avenue, San Francisco, CA 94143.

Patients who may benefit from the SPK procedure must be selected carefully in order to best use scarce organs.

Potential recipients are identified by their nephrologists or endocrinologists and referred to a transplant surgeon for evaluation. Other team members, including transplant nephrologists, nurse coordinators, social workers, and financial counselors, also participate in the initial evaluation. Absolute contraindications to an SPK include active infection, recent or current history of malignancy, and human immunodeficiency virus (HIV) infection. Morbid obesity, advanced cardiovascular or peripheral vascular disease, advanced age, and a history of poor compliance or substance abuse are relative contraindications. Although some centers have reported favorable, SPK results in patients with coronary artery disease who have undergone revascularization,[4] we typically recommend solitary kidney transplant in this patient group. Furthermore, patients must demonstrate a high degree of motivation and an ability to cooperate with the complex protocols for postoperative monitoring and medication.

After a suitable candidate has been identified, we perform an immunologic evaluation, cytomegalovirus, HIV, rapid plasma reagin, human T-lymphotrophic virus I/II and hepatitis serologies, HLA and ABO typing, and panel reactive antibody screening, as well as basic blood chemistries, complete blood count, electrocardiogram (EKG), chest x-ray and coagulation studies. Cardiac evaluation consists of the above EKG, an echocardiogram, and a non-invasive assessment for coronary artery disease. If ischemic heart disease is identified, we request coronary catheterization. Further gastrointestinal evaluation is indicated in patients with a history of peptic ulcer disease or poor gastric emptying. Patients with frequent foot infections or non-healing ulcers warrent a more accurate, non-invasive assessment of the degree of peripheral vascular disease. Patients may also undergo urologic evaluation consisting of a cystourethrogram or possible cystoscopy, depending on their history, and further evaluation by a neurologist is necessary in patients with a history of cerebrovascular disease. Given the long waiting time for transplant, patients must be reevaluated annually to determine any change in their medical status and need for repeat studies.

At the time of admission for transplant, we do a thorough history and physical examination and repeat the laboratories, chest x-ray, and EKG. Any new medical problems or EKG changes may eliminate the patient as a candidate for that particular set of organs. Because we have limited time, once patients are admitted to prepare them for transplant, it is often difficult to do many extra tests to address new medical problems. For this reason, a backup set of patients is often screened for compatibility with any given donor and can be brought in quickly, if the top, potential recipient is deemed unsuitable.

The Surgical Procedure

The first clinically successful SPK transplants were performed at the University of Minnesota in 1966 by Lillihei and Kelly.[5] The first patient developed a pancreatic fistula and rejection, which led to early graft removal and eventual death. The second patient became normoglycemic by the sixth postoperative day and remained so for six months, until she developed a fatal pulmonary infection. This initial report demonstrated the feasibility of pancreas transplantation. There were, however, less than 100 pancreas transplants performed in the next decade, and further advancement in the field was only possible after the improvement of surgical techniques, the introduction of newer immunosuppressants, and the development of a better understanding of pancreas-allograft rejection.

Early technical issues that needed to be resolved included the management of exocrine drainage of the pancreas allograft, the placement of the venous drainage of the allograft, the prevention of graft thrombosis, and the optimum timing of the pancreas transplant in relation to the renal transplant. The management of exocrine drainage was initially accomplished by anastomosing the donor duodenum to a loop of recipient bowel. The use of this technique resulted in a high incidence of anastomotic breakdown with abscess formation and subsequent graft loss. Another technique, the occlusion of the pancreatic duct with injected neoprene, often led to early graft fibrosis. Bladder drainage, whereby the donor's duodenum is anastomosed at the Vater's ampulla directly to the recipient's bladder, has become the most widely accepted technique.[6] This approach permits exocrine secretions to be expelled with the urine and allows for the monitoring of urinary amylase, which is helpful in detecting rejection early in its course. This technique, however, is accompanied by its own set of problems, including fluid and electrolyte, especially bicarbonate, losses; urinary tract complications; and the development of leaks, if the bladder becomes over-distended. Thus, some centers have returned recently to using the technique of enteric drainage and have had more favorable results than before.[7]

The pancreas allograft is now commonly placed in the right iliac fossa with anastomosis of the donor portal vein to the recipient external iliac vein for venous outflow. Arterial inflow is established from the recipient external iliac artery to the superior mesenteric artery and splenic artery of the donor pancreas via an extension graft of donor iliac artery. This results in insulin delivery to the systemic circulation. Careful studies of postprandial glucose metabolism indicate that carbohydrate metabolism remains relatively unaffected, but that a state of hyperinsulinemia is created. This effect appears to be secondary to decreased insulin clearance, because C-peptide levels are not increased.[8] A few groups have questioned this route of insulin delivery and have devised a procedure to allow for anastomosis of the donor portal vein to the recipient portal circulation via the superior mesenteric vein.[9] The benefit of this more physiologic positioning of the graft remains to be seen.[10]

The pancreas graft is a low-flow organ compared to the kidney or liver allograft. Therefore, thrombosis of either the arterial supply or the splenic/portal vein occurred at a significant rate in most centers' early experience.[11] Initial

attempts to decrease rates of graft thrombosis focused on anticoagulation in the early postoperative period. Many programs continue to use aspirin and dipyridamole immediately after surgery. A graft thrombosis rate of less than 5% in most current series has resulted from improvements in preservation solution and organ-recovery techniques, the proper selection of donors and recipients, and better attention to the vascular anastomoses, with proper orientation of the arterial bifurcation graft and shortening of the portal vein to eliminate kinking.

The timing of the pancreas transplant in relation to the renal transplant has also improved. Solitary pancreas transplantation before the development of uremia results in a higher graft loss, secondary to thrombosis. Pancreas transplant after a previous kidney transplant has been performed successfully but is also accompanied by a higher thrombosis rate caused by a lack of uremia. Thrombosis rates are clearly lower when a simultaneous kidney-pancreas transplant is done. Additionally, there are immunologic advantages to the simultaneous transplant procedure. Because concurrent rejection of the kidney and pancreas is seen frequently in recipients of SPK transplants and because rejection of the pancreas can be difficult to diagnose, the parameters of kidney rejection are generally used to trigger the initiation of rejection therapy. Therefore, the presence of a simultaneously-transplanted kidney may result in more prompt treatment of rejection. The recipient of an SPK transplant is also exposed to only one set of HLA antigens; this may have implications regarding sensitization, should re-transplant be necessary. The majority of pancreas transplants have been SPK transplants in the last 15 years. With better immunosuppression, however, solitary pancreas transplantation is becoming more popular, because earlier intervention carries with it the obvious advantage of preventing the secondary complications of diabetes.[12]

The procedure currently used at the UCSF is a culmination of the work and experience outlined above. A successful SPK begins with appropriate donor selection. In general, potential pancreas-kidney cadaver donors tend to be younger; they also have no underlying history of cardiovascular disease or diabetes and no hemodynamic instability during the pre-recovery phase. Donors are typically less than 50 years old, with no absolute cutoff at the lower age limit, although donors weighing less than 45 kg tend to have arterial anatomy of smaller caliber, which may increase the rate of technical complications. A careful medical and social history is obtained, and the ideal donor has no underlying medical conditions that may contribute to pancreatitis, acute tubular necrosis, or infection in the immediate, post-transplant period. Because of the increased need for immunosuppression in SPK recipients, attention to these donor factors is critical.

The recovery operation for the pancreas is a modification of several described techniques. It involves a minimal amount of *in situ* dissection, mostly to mobilize the gland and to identify major vessels, followed by a low-pressure portal and aortic perfusion with University of Wisconsin preservation fluid and subsequent removal of the liver, pancreas and spleen en-bloc. On the back table, in iced solution, the liver and pancreas grafts are carefully separated. The blood supply to each organ is preserved to allow for transplantation. Most arterial anomalies can be handled to accommodate transplantation of both organs,[13] and the meticulous dissection in a cold, bloodless field on the back table allows for identification and preservation of arterial anomalies.

Once the pancreas graft is separated from the liver, the ends of the duodenal segment are trimmed and oversewn. The spleen is removed, and peri-pancreatic tissue is cleared. A culture of the duodenal fluid is obtained to guide postoperative, antibiotic therapy. The splenic artery stump and superior mesenteric artery stump are anastomsed to a Y-graft of donor iliac artery, so that only one arterial anastomosis is necessary in the recipient. The portal vein is mobilized in the donor pancreas to facilitate the venous anastomosis and is kept short to avoid problems with kinks or twists. The time between the cross-clamping of the donor aorta and the implantation of the pancreas graft is kept as short as possible, usually to within 16 hours.

While the recovery team is working on the donor, the recipient will have been selected and brought into the hospital. The preoperative preparation of the recipient consists of several phases. Final cross-matching with current and several earlier recipient serum specimens is completed, using conventional, T-cell cross-matching in non-sensitized patients. Sensitized potential recipients also undergo cross-matching, and in these cases we used fluorescence-activated cell sorter (FACS) cross-matching techniques.[14] The recipient undergoes standard laboratory screening, EKG, and chest x-ray and is given preoperative antibiotics, consisting of vancomycin, fluconazole, and tobramycin, to prevent clinical infections from organisms that frequently reside in the donor duodenum. Enemas are administered until clear, and dialysis is completed if necessary.

Perioperative immunosuppression consists of azathioprine at 4 mg/kg, given in the operating room. One gram of methylprednisolone is also given in the operating room, prior to the administration of the monoclonal antibody Ortho-Clone T-cell 3 (OKT3). Colloid, in the form of albumin, is the preferred intravenous fluid during the procedure, because it appears to minimize graft swelling.

Once the patient is anesthetized, a large-bore Foley catheter, an arterial line, and a central venous catheter are placed. The procedure is performed through a generous mid-line incision. A careful abdominal exploration is done to rule out pathology and assess the status of the iliac vessels. The external iliac artery and vein are mobilized on the left for eventual implantation of the kidney. The right iliac artery and vein are extensively mobilized from the inguinal ligament to the vena cava bifurcation, allowing the vein to be positioned laterally to the artery at the completion of the dissection.

The pancreas graft is implanted first. After completion of the vascular anastomoses, blood sugars are carefully monitored on an hourly basis, because serum-glucose levels typically drop 50 mg/dl each hour and dextrose infusion may be necessary. After the duodenal segment has been anastomosed to the dome of the bladder, allowing exocrine secretions to drain with the urine, the kidney is implanted on the left side with an extra-vesicular bladder anastomosis, using standard techniques (Figure 1). Because SPK donors are carefully selected, the rate of delayed, kidney graft function is less than 5%, and the majority of patients leave the operating room producing urine. Peripancreatic drains are placed prior to closure, which is done in multiple layers. This approach has led to a low level of deep- and superficial-wound infection.[15]

Postoperative patients are monitored in the intensive care unit for 24 hours. A nasogastric tube is left in place until there is evidence of bowel function, and a diet is typically started by postoperative day five. Dipyridamole and aspirin are administered for two to three weeks to reduce the risk of graft thrombosis. After a diet is started, serum glucoses are carefully monitored four times a day. With the exception of one patient, who was subsequently able to discontinue daily insulin injections three months after transplant, patients have not required the perioperative administration of insulin described at some other centers.[16] Once the patient is tolerating a liquid diet, oral immunosuppressive agents are introduced, and thereafter, other medications are converted from intravenous to oral administration. Prophylactic antibiotics are continued for five postoperative days, unless a specific organism is cultured from the donor duodenal segment or from a drain culture. In that case, appropriate antibiotics are continued for two weeks. Drains are typically removed when the drain amylase values have dropped to low levels. Lastly, serum and urine amylase values are monitored daily to detect any evidence of graft pancreatitis, rejection, or other technical problems.

Postoperative immunosuppression consists of methylprednisolone administered in a protocol taper. We administer 5 mg of OKT3 (Orthoclone, Ortho Biotech, New Jersey) daily, until an adequate level of either cyclosporine or tacrolimus is achieved. Azathioprine is continued intravenously at 2 mg/kg until the patient is able to tolerate oral intake, at which time mycophenalate mofetil (MMF) is started at 1.5 grams, twice daily. Either cyclosporine (Neoral, Novartis, New Jersey), or tacrolimus (Prograf, Fujisawa, Japan), is initiated when the patient is tolerating oral intake, and daily levels are followed. Adequate levels are usually achieved by postoperative day ten, and the OKT3 is discontinued. Tacrolimus, MMF (Cellcept, Roche Laboratories, New Jersey) and prednisone have been used more commonly in recent transplants at our center, because we have become more proficient in drug monitoring and the use of this immunosuppressive combination. Several centers have reported a lower rejection rate with this regimen.[17]

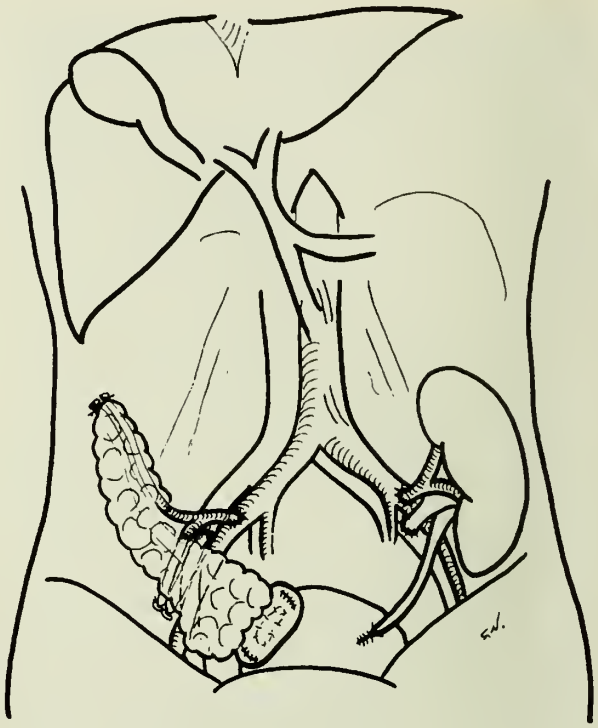


Figure 1.—Schematic diagram of completed pancreas transplant. The pancreas is anastomosed to the external iliac vessels on the right side with the kidney implanted on the left. The exocrine drainage of the pancreas is controlled by anastomosis to the bladder. Alternatively, this anastomosis could be done to the small bowel.

The bladder catheter is left in place for two weeks post-transplant. If patients remain otherwise stable, they can be sent home, once the OKT3 is stopped, and re-admitted for Foley removal. Owing to sodium, bicarbonate, and water loss, hydration status is critical in bladder-drained pancreas patients. Thus, they are typically discharged with an intravenous line in place for at-home saline-administration during the first one to four weeks. Postoperative patients should take in between three and four liters of fluid per day. This goal is more easily met with the at-home use of intravenous (IV) fluid, which has further resulted in fewer early re-admissions for dehydration. The IV is discontinued when the patient can demonstrate a consistent daily oral intake of the required amount of fluid.

Outpatient management consists of frequent clinic visits in the first month after surgery. Laboratory indicators of renal and pancreatic function, including a urinary amylase, are initally followed three times a week. The dosage of prednisone is gradually tapered over the first 6 to 12 months to 10 mg a day, as the patient tolerates. We have recently begun using percutaneous ultrasound-guided biopsies of the pancreas graft to guide rejection therapy, and a system for grading the severity of rejection has been developed.[18]

TABLE 1.—*Reasons for graft and patient loss**

Patient loss	*Kidney Loss*	*Pancreas Loss*
suicide	patient death (2)	patient death (3)
sudden death (2)	rejection	rejection
sepsis	microsporidia infection	microsporidia infection
malignancy	HUS	thrombus
	microangiopathy	infection
	PTLD	

*For 49 patients receiving simultaneous kidney pancreas transplants from 1/95 to 12/96. Overall patient survival was 94% at one year, with kidney and pancreas graft survival of 90% at one year. HUS = hemolytic uremic syndrome, PTLD = Post-transplant lymphoproliferative disorder. Number in parentheses = number of patients. If number not noted = one patient.

Results at UCSF

Since 1989, over 140 SPK transplants have been performed at UCSF, using the above described surgical techniques and perioperative protocols. The biggest changes over the last eight years have involved the types of immunosuppressants used. Induction therapy with OKT3 remains mainstay of our protocol, with MMF and tacrolimus having come into greater use over the last two years. We have reviewed extensively our results in a subset of 49 patients who have received transplants that use these newer immunosuppressive agents. In our review of this subset, we have paid attention to patient and graft outcome, rejection rates, and complication rates.

From January 1995 to December 1996, these 49 patients underwent SPK transplantation at UCSF. The median age of recipients was 38 years, with a range of 24 to 51 years. There were 22 women and 27 men in this subset of patients. All patients had at least 6 months of detailed follow-up.

The overall, one-year patient survival rate was 94%. After one year, the rate of pancreas graft survival, defined as insulin independence, was 90%. There was one loss in the first two weeks due to a graft thrombosis. The rate of kidney graft survival, defined as freedom from dialysis, was also 90%, after one year. The mean creatinine value for patients with one year of followup was 1.5 mg/dl and 1.4 mg/dl at two years. Table 1 shows the reasons for patient and graft losses during the entire, follow-up period.

All patients received OKT3 induction, maintenance prednisone, and various combinations of azathioprine or MMF and cyclosporine or tacrolimus. Rejection of the pancreas was diagnosed by any combination of clinical parameters and laboratory abnormalities, for we have only recently used pancreas biopsies. We considered the following symptoms as potential indicators of pancreas rejection: graft tenderness, fever, sustained fall in urinary amylase to less than half of baseline, rise in serum amylase, or rise in urine eosinophils. Kidney rejection was documented by biopsy in the majority of cases. After 6 months of follow-up, results indicated that 34.7% of these 49 patients were free of rejection, 14.3% had isolated kidney rejection, 12.2% were treated for isolated pancreas rejection, and 28.6% were considered to have had simultaneous pancreatic and renal allograft rejection. Multiple rejections of one or both allografts occurred in 10.2% of these patients. Without biopsy results to confirm pancreas rejection, it is possible that many of the patients classified as having kidney-only rejection may have had concurrent pancreas rejection, but had not yet developed clinical or laboratory signs. Indeed, other centers have reported a much higher rate of concurrent rejection of the two organs.[19] In patients who experienced rejection of either organ in the first six months post-transplant, the mean time to the rejection was 34 days, plus or minus 5.1 days. Rejection treatment consisted of a course of OKT3 for 7 to 10 days in 68.3% of the patients with rejection; the rest received pulsed steroids. Most patients received only a single course of OKT3 for rejection, and more recently, patients undergoing rejection treatment have been given tacrolimus for maintenance immunosuppression.

Complications in the post-transplant period can be divided into technical complications, which usually appear early, and complications of immunosuppression, which often appear later. Only one pancreas graft was lost to thrombosis on postoperative-day 10. During the follow-up period, re-operation for surgical problems directly related to the pancreas and kidney transplant occurred 22 times in 18 patients. Reasons included the repair of leaks at the duodenal segment in 3 patients, conversion to enteric drainage of pancreatic exocrine secretions in 3 patients, lymphocoele drainage in 4 patients, transplant nephrectomy in 3 patients, transplant pancreatectomy in 2 patients, and removal of both grafts in 1 patient. Drainage of an intra-abdominal abscess, repair of a ureteral obstruction, re-exploration for bleeding, and repair of a wound dehiscence each occurred once, and two patients required re-exploration for small bowel obstruction.

Well-recognized complications of immunosuppression include infections and malignancies. During the follow-up period, 26.5% of patients had positive blood or intravenous-line cultures, which required antibiotic treatment. Most of these cultures tested positive for *staphylococcus epidermidis*, and infection had occurred during the initial hospitalization. Frequent urinary tract infections were very common, and 69.4% of patients had at least one positive culture requiring treatment. Most were treated on an outpatient basis with a ten-day course of oral antibiotics. Four patients, however, required hospitalization for urosepsis and treatment with intravenous antibiotics. Recurrent urinary tract infections require both an evaluation with cystoscopy to rule out foreign bodies or stones in the bladder and a determination of the ability of the bladder to empty. Patients with poor bladder function and recurrent urinary infections have been considered for enteric conversion, a procedure whereby the duodenal segment is disconnected from the bladder and anastomosed to the small bowel.

Severe pulmonary infections, one caused by aspergillus, developed in two patients, and in one patient a deep infection developed around the pancreas, with serratia that initially responded to drainage, but ultimately led to graft loss. No superficial-wound infections developed in this series of patients. One patient eventually died with cardiac involvement, as a result of systemic microsporidia infection.

Viral infections continue to be a significant problem in these heavily immunosuppressed patients. Biopsies provided evidence of cytomegaloviral (CMV) infection in the gastrointestinal tract in 8.2% of patients. Blood cultures for CMV were positive in 18.4% of patients, and one patient had evidence of CMV on a kidney biopsy. These CMV infections were typically treated with a three-week course of intravenous ganciclovir. We are greatly concerned about the recent identification of three patients with renal damage, secondary to polyoma viral infections. These patients all presented with a rise in creatinine, which led to biopsy. Histology revealed the characteristic findings of polyoma.[20] There is, unfortunately, no treatment for this virus, and the lowering of immunosuppression has not resolved the infection in these cases.

Malignancies have been relatively unusual in this patient group. One patient developed a post-transplant, lymphoproliferative disorder, which led to kidney loss. This patient was managed with continued, low-dose immunosuppression, consisting of prednisone alone, and has retained pancreas function. A second patient died of metastatic squamous-cell carcinoma of the lung, which had not been identified preoperatively, despite an aggressive work-up of a pleural effusion. We will not know more about the real effect of these newer, more potent immunosuppressants on malignancies until long-term follow-up is available.

We know the readmission rate for SPK recipients to be much greater than that for kidney recipients. This relates to dehydration, metabolic derangements related to the bladder drainage of the duodenal segment, an increased rate of rejection, and an increased rate of infections. During the follow-up period, 96% of patients required readmission. The average number of readmissions was 3.8 per patient, with an average rehospitalization of 19.7 days per patient. These figures emphasize the complex nature of the management of these patients and the need for close, outpatient follow-up.

We further analyzed the last 15 transplants of 1997. Of these patients, 13 received prednisone, MMF, and tacrolimus as maintenance immunosuppression after OKT3 induction. Follow-up time ranges from three to nine months. There have been no patient deaths, no kidney losses, and two pancreas losses due to thrombosis. Rejection occurred in just 4 patients (27%), only 3 of whom required OKT3 therapy. Mean length of stay for the transplant admission was 12.3 days. Readmission was necessary in 73% of these patients, but was generally of a short duration, averaging 11.2 days per patient that required readmission. This drug combination appears to have favorable, early results in terms of graft and patient survival. The long-term effects, as they relate to malignancies and infections, need to be determined.

Effect of SPK on Secondary Complications of Diabetes

The greatest potential benefit of pancreas transplantation is the prevention of secondary complications associated with diabetes. By definition, most patients who undergo SPK transplant have already progressed to end-stage renal disease, owing to diabetic nephropathy. These patients often display features of neuropathy, retinopathy, gastropathy, and diabetic microangiopathy, with a myriad of vascular diseases. The effect of optimal glucose control following pancreas transplantation has been evaluated for its ability either to halt the progression of or reverse some of these complications.

The recurrence of diabetic nephropathy in the transplanted kidneys of patients that did not receive a pancreas transplant has been documented in many series. An increase in the mesangial matrix density is seen in diabetic recipients of isolated kidney transplants, and this lesion is prevented when a pancreas is transplanted simultaneously.[21] Initial reports indicated that a successful, solitary pancreas transplant was unable to reverse the established lesions of diabetic nephropathy in native kidneys.[22] A recent report, however, has documented histologic improvement in the lesions of diabetic nephropathy after a successful, isolated pancreas transplant and resultant normoglycemia of more than five years.[23] In addition, long-term kidney survival rates in SPK recipients tend to be higher than those for diabetic patients receiving only kidneys, perhaps because the quality of the donor kidneys and the underlying health of SPK recipients are often better. The long-term, graft-survival rate has improved, despite a higher, acute rejection rate and higher requirements for increased doses of immunosuppressants.[24]

Retinopathy is often far advanced by the time patients undergo pancreas transplantation. One series, which compared the degree of retinopathy in patients with successful, versus failed, pancreas transplants, reported that there was no difference in visual symptoms over the first three years. After that time, retinopathy stabilized in patients with successful grafts, and patients with failed grafts had further deterioration in their vision.[25] It appears that by the time nephropathy has developed, retinopathy has advanced far enough for the stabilization of retinal lesions to be the best outcome that we can anticipate.[26]

Several studies have evaluated the effect of successful pancreas transplantation on diabetic polyneuropathy.[27–28] Symptomatic improvement and measurable increases in both nerve conduction velocities and sensory action potentials have followed successful pancreas transplantation.[29] Symptoms of gastroparesis often improve as well. It must be remembered, however, that improvement of uremia alone can have an effect on both gastropathy and neuropathy. The degree of autonomic

dysfunction has a negative effect on long-term survival. Survival rates are improving, however, in patients with autonomic dysfunction quantitated by cardiorespiratory reflexes, who have functioning pancreas grafts.[30]

Potential recipients of pancreas-kidney transplants are carefully screened for evidence of cardiovascular disease. It has been shown clearly that there is a high morbidity and mortality rate in patients who have underlying cardiac disease and receive a pancreas transplant.[31] A successful pancreas-kidney transplant may affect the progression of cardiovascular lesions in patients who undergo the procedure and do not have far-advanced, baseline disease. Levels of serum sialic acid, a risk factor for cardiac disease, have been shown to fall more extensively in patients who have receive a successful kidney-pancreas transplant, as opposed to a kidney alone.[32] Carotid lesions were compared in patients following SPK versus isolated kidney transplant. There was a progression of lesions in both groups, but it was less pronounced in the kidney-pancreas recipients.[33] In general, it is difficult to compare these two groups, because many potential kidney-pancreas recipients with advanced cardiac or vascular disease are typically advised to undergo only a kidney transplant. In addition, differences in the progression of disease may be diluted by the adverse effects of increased steroids and hyperinsulinemia in the pancreas-kidney groups.

Pancreas-kidney transplantation alters lipid profiles; there is an increase in HDL cholesterol and a decrease in plasma concentrations of cholesterol and triglycerides.[34] The use of immunosuppressive agents such as cyclosporine and tacrolimus has been associated with worsening lipid profiles in recipients of kidney or liver transplants. It is interesting, however, that lipid profiles improve markedly in SPK patients receiving tacrolimus.[35]

Another advantage of this surgery is the enhanced quality of life enjoyed by patients who receive a successful pancreas-kidney transplant. In a self-reporting questionnaire, patients with a successful transplant reported a more positive health perception, less pain, and greater ability to function socially.[36] In addition, there is a strong willingness on the part of patients with failed grafts to repeat the procedure.

Summary

Simultaneous pancreas-kidney transplantation has evolved over the last 15 years and is now a viable therapeutic option for carefully selected patients. As better drugs become available, both long-term graft- and patient-survival continue to improve, with less rejection and fewer immunosuppressive complications. Overall, the procedure is more complex, has more complications and re-hospitalizations, and a higher incidence of rejection and immunosuppression requirement than renal transplant alone, although these increased risks are diminishing with better patient selection and improvements in technique and postoperative management. The physiologic advantages of near-perfect glucose metabolism and its potential effect on the progression of diabetic complications, as well as overwhelming patient satisfaction, appear to justify these increased risks. Further developments in solitary pancreas transplantation will, we hope, allow for earlier intervention in the natural history of diabetes. In the meantime, all physicians in the field of pancreas transplantation await a practical and successful technique for transplanting islet tissue alone, although this goal remains out of reach.

REFERENCES

1. Harris M, Hadden WC, Knowles WC, Bennett PH. Prevalence of diabetes and impaired glucose tolerance and plasma glucose levels in the United States population aged 20–74 years. Diabetes 1987; 36:523–534

2. Nathan DM. Long-term complications of diabetes mellitus. New Engl J Med 1993; 328:1676–1684

3. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin dependent diabetes mellitus. New Engl J Med 1993; 329:977–986

4. Schweitzer EJ, Anderson L, Kuo P, et al. Safe pancreas transplantation in patients with coronary artery disease. Transplantation 1997; 63:1294–1299

5. Lillehei RC, Idezuki Y, Feemster JA, et al. Transplantation of stomach, intestine and pancreas: Experimental and clinical observations. Surgery 1967; 62:721–741

6. Sollinger HW, Ploeg RJ, Eckhoff DE, et al. Two hundred consecutive simultaneous pancreas-kidney transplants with bladder drainage. Surgery 1993; 114:736–744

7. Corry RJ, Egidi MF, Shapiro R, et al. Pancreas transplantation with enteric drainage under tacrolimus induction therapy. Transplantation Proc 1997; 29:642

8. Matte J, Fery F, Lankoande C, Schinohoritis P, De Pauw L. Insulin secretion and glucose tolerance evolution in kidney-pancreas graft. Transplantation Proc 1995; 27:3073–3074

9. Gaber AO, Shokouh-Amiri MH, Grewel HP, Britt LG. A technique for portal pancreas transplantation with enteric drainage. Surg Gynecol Obstet 1993; 177:417

10. Newell KA, Woodle ES, Millis JM, et al. Pancreas transplantation with portal venous drainage and enteric exocrine drainage offers early advantages without compromising safety or allograft function. Transplantation Proc 1995; 27:3002–3003

11. Troppmann C, Gruessner AC, Benedetti E, et al. Vascular graft thrombosis after pancreatic transplantation: Univariate and multivariate operative and non-operative risk factor analysis. J Am Coll Surg 1996; 182:285–316

12. Bartlett ST, Schweitzer EJ, Johnson LB, et al. Equivalent success of simultaneous pancreas kidney and solitary pancreas transplantation. Ann Surg 1996; 224:440–452

13. Mizrahi SS, Jones JW, Bentley FR. Preparing for pancreas transplantation: donor selection, retrieval technique, preservation, and back-table preparation. Transplantation Rev 1996; 10:1–12

14. Pelletier RP, Orosz CG, Adams PW, et al. Clinical and economic impact of flow cytometry cross-matching in primary cadaveric kidney and simultaneous pancreas-kidney transplant recipients. Transplantation 1997; 63:1639–1645

15. Freise CE, Stock PG, Roberts JP, Melzer JS. Low postoperative wound infection rates are possible following simultaneous pancreas-kidney transplantation. Transplantation Proc 1995; 27:3069–3070

16. Troppmann C, Gruessner AC, Papalois BE, et al. Delayed endocrine pancreas graft function after simultaneous pancreas-kidney transplantation. Transplantation 1996; 61:1323–1330

17. Gruessner RW, Sutherland DER, Drangstveit MB, Troppmann C, Gruessner AC: use of FK506 in pancreas transplantation. Transplant Int 1996; 9(Suppl 1):S251–S257

18. Drachenberg CB, Papadimitriou JC, Klassen DK, et al. Evaluation of pancreas transplant needle biopsy. Transplantation 1997; 63:1579–1586

19. Pappo O, Demetris AJ, Raikow RB, Randhawa PS. Human polyoma virus infection of renal allografts: histopathologic diagnosis, clinical significance, and literature review. Modern Pathol 1996; 9:105–109

20. Allen RDM, Wilson T, Grierson G. Percutaneous biopsy of bladder-drained pancreas transplants. Transplantation 1991; 51:1213

21. Wilczek HE, Jaremko G, Groth CG. Evolution of diabetic nephropathy in kidney grafts. Transplantation 1995; 59:51–57

22. Fioretto P, Mauer MS, Bilous RW, Goetz FG, Sutherland DER, Steffes MW. Effects of pancreas transplantation on glomerular structure in insulin-dependent diabetic patients with their own kidneys. Lancet 1993; 342:1193–1196

23. Fioretto P, Steffes M, Sutherland DER, Goetz F, Mauer M. Reversal of lesions of diabetic nephropathy after pancreas transplantation. New Engl J Med 1998; 339:69–75

24. El-Gebely S, Hathaway DK, Elmer DS, Gaber LW, Acchiardo S, Gaber AO. An analysis of renal function in pancreas-kidney and diabetic kidney-alone recipients at two years following transplantation. Transplantation 1995; 59:1410–1415

25. Ramsey RC, Goetz FC, Sutherland DER, et al. Progression of diabetic retinopathy after pancreas transplantation for insulin-dependent diabetes mellitus. New Engl J Med 1988; 318:208–214

26. Sutherland DER. Effect of pancreas transplants on secondary complications of diabetes: review of observations at a single institution. Transplantation Proc 1992; 24:859–860

27. Laftavi MRA, Chapuis F, Vial C, et al. Diabetic polyneuropathy outcome after successful pancreas transplantation:1 to 9 year follow up. Transplantation Proc 1995; 27:1406–1409

28. Trojaborg W, Smith T, Jakobsen J, Rasmussen K. Effect of pancreas and kidney transplantation on the neuropathic profile in insulin-dependent diabetics with end-stage nephropathy. Acta Neurologica Scandinavica 1994; 90:5–9

29. Muller-Felber W, Landgraf R, Scheuer R, et al. Diabetic neuropathy 3 years after successful pancreas and kidney transplantation. Diabetes 1993; 42:1482–1486

30. Navarro X, Kennedy WR, Loewenson RB, Sutherland DER. Influence of pancreas transplantation on cardiorespiratory reflexes, nerve conduction, and mortality in diabetes mellitus. Diabetes 1990; 39:802–805

31. Manske CL, Wang Y, Thomas W. Mortality of cadaveric kidney transplantation versus combined kidney-pancreas transplantation in diabetic patients. Lancet 1995; 346:1658–1662

32. Auersvald LA, Perez RV, Lorber MI, et al. Serum sialic acid, a risk factor for cardiovascular disease, improves following pancreas transplantation. Transplantation Proc 1995; 27:3037

33. La Rocca E, Minicucci F, Secchi A, et al. Evolution of carotid vascular lesions in kidney-pancreas and kidney-alone transplanted insulin-dependent diabetes patients. Transplantation Proc 1995; 27:3072

34. Foger B, Konigsrainer A, Palos G, et al. Effects of pancreas transplantation on distribution and composition of plasma lipoproteins. Metabolism 1996; 45:856–861

35. Burke GW, Alejandro R, Roth D, et al. Use of FK506 in simultaneous pancreas/kidney transplantation: Lack of impairment of glycemic or lipid metabolism. Transplantation Proc 1995; 27:3119–3120

36. Gross CR, Zehrer CL. Health-related quality of life outcomes of pancreas transplant recipients. Clin Transplantation 1992; 6:165–171

Articles

Research Interests of Physicians in Two Practice-Based Primary Care Research Networks

MARY S. CROUGHAN-MINIHANE, PhD; *San Francisco, California;* DAVID H. THOM, MD, PhD; *Palo Alto, California; and* DIANA B. PETITTI, MD, MPH; *Pasadena, California*

Regional practice-based network research has grown significantly in the past 15 years. Previous studies have reported on characteristics of physicians who participate in network research, but little is known about the specific *a priori* research interests of practicing physicians. Knowledge of such interests could be useful in planning network research studies. We conducted a mail survey to assess the research interests of primary care physicians in two contiguous research networks at the University of California at San Francisco (UCSF) and at Stanford University. Among 120 respondents from the UCSF Collaborative Research Network and 85 from the Stanford Ambulatory Research Network, the most common topics of interest were disease prevention, communication and compliance, and managed care. Among specific conditions, heart disease, hypertension, and respiratory infection were of interest to the majority of respondents. Topics not of interest to network members were obstetrics, diagnostic procedures, alcoholism, drug abuse, tuberculosis, male genito-urinary problems, occupational hazards, domestic violence, and AIDS and HIV. Identification of network physician research interests can help focus research and recruitment efforts on topics of interest and provide estimates of participation levels for planning studies and preparing funding applications for research networks.

(Croughan-Minihane MS, Thom DH, Petitti DB. Research interests of physicians in two practice-based primary care research networks. West J Med 1999; 170:19–24)

Conducting research using primary care practice-based networks has been promoted for several reasons. The primary reason is that research from academic settings often fails to address the clinical questions that are most important to primary care physicians who see patients as a full time occupation.[1,2] In addition, primary care research can be difficult in academic settings because of the relatively small primary care base that may not be representative of the surrounding community.

Practice-based networks, while not necessarily representative of all practices, are believed to be more representative than outpatient clinics in medical centers or referral clinics.[3] The representative nature of practice-based research has several advantages. First, it allows the study of diseases in patients as they present to the primary care physician, rather than a subset of patients selected for referral on the basis of difficult or unrepresentative problems. This is an important advantage when studying diseases such as asthma, which have a broad spectrum of severity, with the "base of the iceberg" seen only in the primary care setting. Second, it allows the study of diseases, and their treatment, in a setting similar to the target setting for the study's results. Finally, studies of clinical decision-making in community practice settings can provide insights for incorporation into the development of practice guidelines and serve as a testing site for implementation.[4]

A recent review listed 28 active practice networks in North America.[5] Previous publications have provided more detailed information on individual networks, including the Dartmouth COOP Project,[6] the Ambulatory Sentinel Practice Network,[7] the Upper Peninsula Research Network,[8] the Wisconsin Research Network,[9] and the University of California, San Francisco (UCSF), Collaborative Research Network.[10] The structure and nature of the various networks differ. For example, the Upper Peninsula Research Network is composed of family physicians who teach or precept students from the Upper Peninsula Campus of the Michigan State University College of Human Medicine.[8] In contrast, the Wisconsin Research Network was established by the Wisconsin Academy of Family Physicians, and participating

From the Department of Family and Community Medicine (Drs Croughan-Minihane and Petitti), the University of California, San Francisco; the Department of Medicine (Dr Thom), Division of Family Medicine, Stanford University, Palo Alto. Dr Petitti is now with the Division of Research and Evaluation, Kaiser Permanente, Pasadena, California.

Reprint requests to Dr. Mary Croughan-Minihane, Department of Family and Community Medicine, MU-3E, Box 0900, University of California, San Francisco, CA 94143-0900 (e-mail: mscroug@itsa.ucf.edu).

primary care physicians are drawn from practicing physicians throughout the state, without regard to academic ties.[9]

While the articles cited above have provided details on the structure of various networks, and their accomplishments have been highlighted in original research publications,[11–19] little has been published about the research interests of primary care physicians within the various networks. We believe that knowing the research interests of network physicians is critical to performing individual studies. Personal interest in the topic, relevance to one's practice, and "buying in" to the study enhances the research experience of the physician and facilitates conduct of the study. A previous study[10] of one of our networks found that 40% of family physicians serving on the clinical faculty were interested in participating in collaborative research, with more than half of the physicians willing to participate in randomized trials (63%), patient surveys (60%), evaluation of physician practices (59%), patient referral to research conducted elsewhere (54%), or chart reviews (53%). To our knowledge, no study has assessed network physician interest in specific research topics. The purpose of our study was to characterize physicians and their practices and to determine specific research interests, thereby assessing the feasibility of conducting collaborative research on particular topics and enhancing linkages between investigators and practicing physicians with similar research interests.

Methods

Network Development

Two geographically contiguous, nonoverlapping, collaborative research networks have evolved in the Greater San Francisco Bay Area of California: the UCSF Collaborative Research Network of the Department of Family and Community Medicine at UCSF, and the Stanford Ambulatory Research Network of the Division of Family Medicine at Stanford University. Membership in one network precludes membership in the other.

In 1984, a faculty member (D.B.P.) in the Department of Family and Community Medicine at UCSF began to identify office-based physicians in the greater San Francisco Bay area who had an interest in participating in practice-based research.[10] Physicians with volunteer clinical appointments in the department were the primary source of physician members of the network. Membership was supplemented by personal referral from other physicians and faculty. A number of primary care internists with clinical appointments in the Department of Medicine were added to the pool of network physicians in 1986. The UCSF Network currently is governed by an advisory committee, which comprises practice-based physicians who are members of the Network and university-based researchers in the Department of Family and Community Medicine. A semi-annual newsletter is sent to each participating physician as a method of maintaining interest and as a recruiting device.

A faculty member (D.H.T.) in the Division of Family Medicine at Stanford University surveyed all identified office-based family practice physicians in the local area (i.e., Santa Clara and southern San Mateo counties) to ascertain physicians who were interested in participating in office-based research. Physicians were identified from the *1993 Directory of Diplomates, American Board of Family Practice, the American Academy of Family Physicians 1992–93 Membership Directory*, the county medical associations for the geographic area surveyed, and current business listings for family practice and general practice in local telephone directories. Excluded from the list were family medicine residents and family physicians in residency or university-based practices ($n = 12$). Of the 307 physicians sent surveys, 206 (67%) responded after two mailings, of which 176 physicians (85%) were in practice. Among the 176 responding physicians, 85 (48%) stated that they were interested in office-based research. These 85 primary care physicians made up the new Stanford Ambulatory Research Network.

Survey Methodology

After formation of the UCSF Collaborative Research Network, it became necessary to update membership enrollment and information in the network database on a regular basis. D.B.P. and M.S.C.-M. assembled a new list consisting of physicians with active, unpaid appointments on the clinical faculty in the Department of Family and Community Medicine at UCSF and primary care physicians who had previously participated in department-sponsored practice-based studies. Physicians with specialty certification in pediatrics, surgery, psychiatry, and obstetrics and gynecology were then excluded (unless the physician was also certified in family practice or internal medicine). A mailed survey was sent to the 347 physicians who made up the list. Responses to this survey and phone follow-up were used to determine whether each physician was eligible to be a member of the UCSF Network by virtue of being involved in the delivery of primary care services and, if eligible, whether he or she was interested in participating in practice-based research. Of the 347 physicians surveyed by UCSF, 27 had moved and could not be located and 43 were not involved in primary care. Of the remaining 277 physicians, 55 (20%) did not respond to two mailings and a phone follow-up, and 102 physicians stated they were not interested in practice-based research.

The 120 eligible physicians with an interest in practice-based research completed a survey asking for information on themselves, the organization of their practice, and the characteristics of the patients in their practice. Previous research with a subgroup of these physicians indicated that their estimates of practice characteristics were valid when compared with an on-site audit (unpublished data). They were also asked to rate their level of interest in participating in research on each of 34 topic areas on a 1 to 5 Likert scale (1 = very interested, 5 = not at all interested). The topic areas were stated as short phrases, and included specific diseases or conditions (e.g., tuberculosis, domestic violence), specific patient subpopulations (e.g., adolescent

TABLE 1.—*Physician and Practice Characteristics for Members of the UCSF and Stanford Networks**

	UCSF	Stanford
n	120	85
Age (years)	45 ± 8	45 ± 11
Sex (M/W)	104/16	59/26
Graduated from medical school after 1975	57	54
Board-certified	96	80
Specialty		
Family medicine	75	93
Internal medicine	11	1
Other	14	6
Group practice	64	68
Patient visits per week	97 ± 44	97 ± 37

*Data are means ± SD or %.

medicine), and areas related to the process of medical care (e.g., computerized medical records). The 120 responding physicians made up the new and ongoing members of the UCSF Collaborative Research Network.

A modified version of the UCSF survey instrument was completed by the 85 physicians who indicated an interest in office-based research in the survey of family physicians done by Stanford University. In addition, this survey contained an open-ended question asking physicians for additional research topics in which they were interested in participating.

Analytic Strategy

Responses from the UCSF and Stanford surveys were entered into individual databases at each site, then merged into a single database. When identical questions were asked on each of the two surveys, answers were coded in an identical manner. When survey questions differed, common categories were developed for the two surveys. Categorical variables were analyzed using the χ^2 statistic and Fisher's exact test. Continuous variables with normal distributions were analyzed using Student's *t* test and analysis of variance. The Wilcoxon rank sum test was used to test the significance of differences in scales of research topic interest, because the scales were not normally distributed.

Results

The demographic characteristics and practice characteristics of physician members of the UCSF Collaborative Research Network and the Stanford Ambulatory Research Network (Table 1) are quite similar with regard to physician's mean age, time since medical school graduation, proportion in group practice, and patient volume. A slightly larger proportion of Stanford Network members are women (26% versus 16%) and fewer Stanford Network members are board certified (80% versus 96%). The UCSF Network has greater diversity in board certification.

TABLE 2.—*Average Physician Estimates of Patient Age, Ethnicity, and Payment Arrangement Categories for the UCSF and Stanford Networks**

	UCSF	Stanford
n	120	85
Patient age categories		
Children (≤13 years)	12 ± 1	14 ± 1
Adolescents (14–18 years)	8 ± 1	10 ± 1
Adults (19–64 years)	60 ± 2	58 ± 2
Older adults (≥65 years)	19 ± 2	18 ± 2
Patient ethnic categories (%)		
Non-Hispanic white	61 ± 3	63 ± 2
Hispanic	19 ± 2	18 ± 2
Asian/Pacific Islander	9 ± 1	13 ± 2
African American	8 ± 1	5 ± 1
Other	1 ± 0	1 ± 1
Payment arrangement categories (%)		
Fee for service	32 ± 2	19 ± 2
Prepaid private insurance	25 ± 2	50 ± 3
No insurance	13 ± 2	10 ± 2
Medicare	9 ± 1	12 ± 1
Medicaid	14 ± 2	6 ± 2
Other	3 ± 1	3 ± 1

*Data are mean % ± SE. Percentages do not always add to 100: not all of the original physician estimates totaled 100% and results were rounded.

Physician estimates of the distribution of patient age categories, ethnic categories, and payment arrangement categories are provided in Table 2. The majority of patients are estimated to be between 19 and 64 years of age, with nearly identical age distributions between the UCSF and Stanford networks. More than 60% of patients in both networks are reported to be non-Hispanic white. Patient payment arrangements are significantly different: Stanford Network members estimated a higher proportion of prepaid private insurance patients (50% versus 25%) and a lower proportion of fee for service (19% versus 32%) and Medicaid patients (6% versus 14%) than UCSF Network members.

Table 3 indicates the percentage of network members who indicated that they were interested or very interested (scores of 1 or 2 on a 5-point scale) in a particular research topic, either specified on the questionnaire or that they chose to write in. We categorized the topics according to five general groupings for ease of interpretation. The "other interests" category yielded 26 separate interest areas, of which only one (sexually transmitted diseases) was suggested by three respondents; another six topics were suggested by two physicians each.

Relatively high percentages of physicians in both networks were interested in a variety of topics. When the same topics were listed on both surveys, members of the two networks ranked them similarly. In addition, the top five interests in both networks were similar: smoking cessation, doctor-patient communication, hypertension,

TABLE 3.—*Research Topics of Interest to Network Members**

	UCSF	Stonford
n	120	85
Disease prevention and health education		
Alcoholism	22.2	—
Diet/dietary change	50.5	—
Disease prevention	—	78.0
Domestic violence	—	27.5
Drug abuse	27.6	—
Health education	51.4	70.6
Occupational hazards	29.0	—
Smoking	57.7	—
Doctor-patient relationships		
Doctor-patient communication	57.1	65.9
Patient compliance	—	52.5
Psychosocial care	27.8	—
Specific Patient Populations		
Adolescent medicine	29.3	—
Geriatrics	39.4	—
Gynecology	42.0	—
Obstetrics	31.7	—
Pediatrics	35.4	—
Sports medicine	37.6	—
Practice and practice management		
Computer/records	40.0	—
Diagnostic procedures	47.2	—
General office medicine	54.1	—
Lab tests/results	38.0	—
Managed care	—	51.8
Organizational/practice	40.5	—
Payment/economics	39.0	—
Quality assurance	48.5	—
Specific conditions		
AIDS/HIV	28.7	26.0
Arthritis	26.3	—
Cancer	32.0	—
Diabetes	49.5	—
Heart disease	44.4	50.6
Hypertension	56.4	54.9
Male genito-urinary problems	30.3	—
Obesity and management	34.3	—
Osteoporosis	—	45.1
Pain management	39.4	49.4
Peptic ulcer/dyspepsia	—	40.2
Respiratory infections	—	53.0
Sexually transmitted disease	33.3	—
Tuberculosis	23.7	—
Upper respiratory infection	30.3	
Urinary incontinence	—	29.3
Urinary tract infection	32.0	—

*Data are %.

general office medicine, and patient education were the top five interests for UCSF Network members while disease prevention, health education, doctor-patient communication, hypertension, and respiratory infections were the top five interests for Stanford Network members. Examining the median scores for the four broad categories of interest that contained responses from members of both networks, the highest interest was in research on practice and practice management (median score 2.7 for UCSF and 2.0 for Stanford), followed by disease prevention and health education (2.8 for UCSF and 2.3 for Stanford), specific disease conditions (2.9 for both UCSF and Stanford), and doctor-patient relationships (3.5 for UCSF and 2.2 for Stanford).

Exploratory analyses were conducted to compare research interests of physicians by specialty (internal medicine vs. family practice), percent of patients in managed care (above or below group median), previous research experience, and sex. Differences in research interests by specialty were consistent with the differences in patient populations seen: family physicians were more interested in obstetrics-gynecology and pediatric topics. Percent of patients in managed care did not appear to have any consistent influence on topics chosen. Physicians with previous research experience reported a greater interest in specific condition topics as a group ($P = 0.01$) that reflected a slightly greater interest in virtually every topic listed. Male and female physicians were generally similar in the proportion interested or very interested in each topic, with the exceptions of osteoporosis (62% women versus 39% men, $P = 0.06$), urinary incontinence (50% women versus 22% men, $P = 0.01$), health education (86% women versus 65% men, $P = 0.06$), and patient-physician communication (71% women versus 46% men, $P = 0.04$).

Since it is equally important to note specific topics *not* of interest to a large proportion of network members, Table 4 presents the percentage who indicated that they were not or not at all interested in a particular topic (scores of 4 or 5 on a 5-point scale). Overall, generally low percentages of physicians in both networks indicated that they were not interested in specific topics. Research topics that were not of interest to more than 40% of UCSF Network members were obstetrics, diagnostic procedures, alcoholism, drug abuse, tuberculosis, male genito-urinary problems, occupational hazards, and AIDS and HIV. Although a smaller number of topics was offered to Stanford Network members, more than 40% were not or not at all interested in only AIDS and HIV and domestic violence.

Of UCSF Network members, 67% had participated in at least one research study in the past, 33% in two or more; 48% of Stanford Network members had participated in at least one research study in the past. Members' responses to queries on factors influencing the likelihood of research participation were very similar between the networks. Approximately 50% felt that continuing medical education credit, fulfillment of clinical faculty appointment hour requirements, or paid honoraria would increase or greatly increase their likelihood of participating in studies. Thus approximately 50% would not have their participation influenced by any of these factors.

TABLE 4.—*Research Topics Not of Interest to Network Members**

	UCSF	Stonford
n	120	85
Disease prevention and health education		
Alcoholism	49.5	—
Diet/dietary change	25.7	—
Disease prevention	—	7.4
Domestic violence	—	41.3
Drug abuse	49.0	—
Health education	15.3	10.6
Occupational hazards	42.0	—
Smoking	18.2	—
Doctor-patient relationships		
Doctor-patient communication	17.2	9.7
Patient compliance	—	8.7
Psychosocial care	36.1	—
Specific patient populations		
Adolescent medicine	37.3	—
Geriatrics	32.3	—
Gynecology	26.0	—
Obstetrics	58.6	—
Pediatrics	36.5	—
Sports medicine	38.6	—
Practice and practice management		
Computer/records	37.2	—
Diagnostic procedures	50.8	—
General office medicine	18.4	—
Lab tests/results	27.0	—
Managed care	—	19.3
Organizational/practice	32.7	—
Payment/economics	37.2	—
Quality assurance	25.8	—
Specific conditions		
AIDS/HIV	41.6	45.5
Arthritis	35.4	—
Cancer	29.9	—
Diabetes	26.2	—
Heart disease	24.2	13.5
Hypertension	14.9	15.9
Male genito-urinary problem	42.4	—
Obesity and management	27.8	—
Osteoporosis	—	23.2
Pain management	35.6	21.7
Peptic ulcer/dyspepsia	—	23.2
Respiratory infections	—	16.8
Sexually transmitted disease	25.3	—
Tuberculosis	46.4	—
Upper respiratory infections	30.3	—
Urinary incontinence	—	34.2
Urinary tract infection	24.8	—

*Data are %.

Discussion

Identification of network physician research interests *a priori* can help focus research and recruitment efforts on topics of interest and provide estimates of participation levels for study planning and grant proposals. It is notable, though perhaps not surprising, that for physicians from both the UCSF and Stanford networks, the topics of interest to the greatest proportion of physicians were generally concerned with non–disease-specific areas of disease prevention, communication and compliance, and managed care. Among specific conditions, only three of the most common conditions (heart disease, hypertension, and respiratory infection) were chosen by >50% of respondents. Additional areas of potentially greater interest to researchers and funding agencies, namely domestic violence, AIDS, alcoholism, drug abuse, tuberculosis, and urinary incontinence, were relatively unpopular, being chosen by <30% of respondents.

Asking physicians to rank their interests from a list of topics, as was done in the current study, has the advantage of specificity of responses, thereby avoiding the dispersion of topics that might occur with an open-ended format. In the Stanford survey, an additional question asking for other topics of interests yielded 26 separate interest areas, of which only one (sexually transmitted diseases) was suggested by three respondents.

It is important to note that interest in a topic area is not synonymous with willingness to participate in a specific study. The latter would likely depend on the specific hypothesis, methods employed, and resources required to participate. To the extent self-reported interests reflect physician willingness to participate in specific studies, this information can prove quite helpful to networks as they plan studies and prepare funding applications.

The representative nature of practice-based research networks with regard to other physicians interested in primary care research, as well as those in office-based practice, has been addressed previously.[19] The UCSF and Stanford networks are two relatively small, similar research networks located in a single geographic area. As such, the results may not be generalizable to geographically dispersed networks or networks in areas with less managed care. For example, the proportion of our network members in group practices is nearly double the national figure. Members of the UCSF and Stanford networks do, however, have characteristics comparable to national norms provided for family physicians, general practitioners, and general internists[20] with regard to physician demographic characteristics and average number of patient visits per week. Our network member characteristics are also comparable to those of members of Ambulatory Sentinel Practice Network, a binational practice-based primary care research network comprised of 72 practices in the United States.[21] Furthermore, Ambulatory Sentinel Practice Network members have been found to be comparable to general and family practices included in the National Ambulatory Medical Care Survey,[19] although patients seen by our Network members represent a more ethnically diverse population than do the Ambulatory Sentinel Practice Network or the National Ambulatory Medical Care Survey.

Physician and practice characteristics have been reported in the current study to allow the reader to compare

results of our study with the research interests of other network physicians. The 120 members of the UCSF Collaborative Research Network and the 85 members of the Stanford Ambulatory Research Network are primarily in small group practices, serving predominantly non-Hispanic white populations in private, prepaid, or fee-for-service settings. This broad-brush portrait, however, belies the diversity of the physicians, their patients, and their practices. Also diverse are the interests of the physicians in various topics that are of importance in primary care. The diverse nature of the physicians, practices, and patients, coupled with their high level of interest in research participation, suggests that the groups constitute a rich resource for conduct of practice-based research.

Acknowledgments

Funding for this study was provided by the Health Resources Services Administration Grants for the Establishment of Departments of Family Medicine (2 D32 PE19036-04). We would like to thank Dr. William Fowkes, Elaine Woodard, Heather Wilkie, and Elizabeth Dito for their support and assistance with these studies.

REFERENCES

1. Estes EH. Primary care research. Where have we been? Where are we going? In Mayfield J, Grady ML (Eds): Primary Care Research: An Agenda for the 90s. Rockville, MD, Agency for Health Care Policy and Research, 1990, pp 5–8

2. Green LA, Lutz LJ. Notions about networks: primary care practices in pursuit of improved primary care. In Mayfield J, Grady ML (Eds): Primary Care Research: An Agenda for the 90s. Rockville, MD, Agency for Health Care Policy and Research, 1990, pp 125–132

3. Nutting PA, Alexander GP. Conducting clinical trials in practice settings. Research in progress by family physicians. J Fam Pract 1992; 35:689–691

4. Green LA. How can family practice and primary care practice-based research networks contribute to medical effectiveness research? In Hibbard H, Nutting PA, Grady ML (Eds): Primary Care Research: Theory and Methods. Rockville, MD, Agency for Health Care Policy and Research, 1991, pp 283–286

5. Niehauer L, Nutting PA. Primary care practice-based research networks active in North America. J Fam Pract 1994; 38:425–426

6. Nelson EC, Kirk JW, Bise BW, et al. The Cooperative Information Project: Part 1: a sentinel practice network for service and research in primary care. J Fam Pract 1981; 13:641–649

7. Green LA, Wood M, Becker LA, et al. The Ambulatory Sentinel Practice Network: purpose, methods, and policies. J Fam Pract 1984; 18:275–280

8. Hickner J. Practice-based primary care research networks. In Hibbard H, Nutting PA, Grady ML (Eds): Primary Care Research: Theory and Methods. Rockville, MD, Agency for Health Care Policy and Research, 1991, pp 13–22

9. Beasley JW, Cox NS, Livingston BT, et al. Development and operation of the Wisconsin Research Network. Wisc Med J 1991; 90:534–537

10. Osborn EHS, Petitti DB. Physician interest in collaborative research. J Am Board Fam Pract 1988; 1:29–32

11. Root DT, Hickner JM, Nelson TC. Prevalence and prediction of chlamydial cervical infection in a rural area: an UPRNet project. J Fam Pract 1991; 33:369–374

12. Petitti DB, Grumbach K. Variation in physicians' recommendations about revisit interval for three common conditions. J Fam Pract 1993; 37:235–240

13. Croughan-Minihane MS, Petitti DB, Rodnick JR, Eliaser G. Clinical trial examining effectiveness of three cough syrups. J Am Board Fam Pract 1993; 6:109–115

14. Wasson JH, O'Connor GT, James DH, et al. A physician-completed patient registry system: pilot results for unstable angina in the elderly. J Gen Intern Med 1992; 7:298–303

15. Change HJ, Bell JR, Deroo DB, et al. Physician variation in anticoagulating patients with atrial fibrillation. Arch Intern Med 1990; 150:81–84

16. Herman-Giddens ME, Slora EJ, Wasserman RC, et al. Secondary sexual characteristics and menses in young girls seen in office practice: a study from the Pediatric Research in Office Settings network. Pediatr 1997; 94:505–512

17. Hahn DL, Beasley JW. Diagnosed and possible undiagnosed asthma: a Wisconsin Research Network (WReN) study. Wisconsin Research Network (WReN) Asthma Prevalence Study Group. J Fam Pract 1994; 38:373–379

18. Triezenberg DJ, Smith MA, Holmes TM. Cancer screening and detection in family practice: a MIRNET study. J Fam Pract 1995; 40:27–33

19. Green LA, Miller RS, Reed FM, Iverson DC, Barley GE. How representative of typical practice are practice-based research networks? A report from the Ambulatory Sentinel Practice Network Inc (ASPN). Arch Fam Med 1993; 2:939–949

20. American Academy of Family Physicians. Facts Book, Kansas City, Mo, 1995

21. Ambulatory Sentinel Practice Network Convocation materials, Denver, Colo, 1995

Relationship Between Earlier and Later Mammography Screening—California Medicare, 1992 Through 1994

JENNIFER D. PARKER, PhD; *Hyattsville, Maryland*; FABIO SABOGAL, PhD; *and* TEBEB GEBRETSADIK, MPH; *San Francisco, California*

Regular screening mammography is recommended to reduce breast cancer mortality. Although predictors of mammography have been studied, factors that influence adherence to guidelines are less understood. We examined the relationship between an index mammogram and subsequent mammograms among California Medicare beneficiaries. Medicare billing data for 1992, 1993, and 1994 were used to estimate the association between screening mammography in 1992 and subsequent screening in 1993 or 1994. We found that women with a 1992 mammogram were more than twice as likely to have a mammogram in 1993 or 1994 than women without a 1992 mammogram (relative risk = 2.58; 95% confidence interval, 2.57–2.59). This relationship was somewhat stronger for black women compared with white women and increased with age. Although further study of regular screening patterns is needed, these findings provide some evidence that encouraging a single mammogram may lead to continued adherence.

(Parker JD, Sabogal F, Gebretsadik T. Relationship between earlier and later mammography screening—California Medicare, 1992 through 1994. West J Med 1999; 170:25–27)

Screening mammography significantly reduces breast cancer mortality in women 50 to 74 years of age.[1,2] As a result, routine mammography screening for women older than 40 years is widely recommended.[2,3]

Despite Medicare coverage for biennial screening mammography between 1991 and 1997 (as of January 1998, Medicare covers annual screening mammograms), fewer than 40% of eligible beneficiaries had at least one mammogram in a two-year period.[4] Several studies have documented predictors of screening mammography in the Medicare population,[5–8] but less is known about subsequent screening among these women.[9–11] A recent study of low-income women found that 45% had subsequent screening mammography during the 15-month follow-up.[9] A different study of women older than 40 years found a single screening mammogram was the strongest predictor of screening two years later.[11]

We examined the relationship between mammography in a single year and mammography in a subsequent two-year period among a large group of California Medicare beneficiaries. Knowledge about the relationship between a single mammogram and subsequent screenings at recommended intervals provides insight into the possible long-term effects of outreach efforts and an indication of how useful an index of mammography screening during a single year is for inferences about future screening.

Methods

We used billing data from the Health Care Financing Administration for 1992, 1993, and 1994 to identify mammograms among Medicare beneficiaries in California. Our study population began with 1,360,448 female beneficiaries aged 65 years or older in January 1992 and alive through December 1994. We excluded women enrolled in a health maintenance organization at any time during the three years (37%) because the Health Care Financing Administration does not receive bills for services provided under managed care contracts. We also excluded women who had more than one mammogram during any six-month period between 1992 and 1994. This exclusion was made to reduce potential bias of including women with clinical indications that require screening mammography at closer intervals (about 1%). Our final study group comprised 845,442 California women.

Our main predictor, earlier screening mammography, was defined as at least one mammogram in 1992. Our outcome measure, later screening mammography, was defined as at least one mammogram in 1993 or 1994. All mammograms were combined for this analysis because screening and diagnostic mammography claims are difficult to distinguish in Medicare files.[4] Although race is available from the Medicare file, coding for groups other

From the California Medical Review, Inc, San Francisco. Dr Parker is now with the National Center for Health Statistics, Hyattsville, Maryland.
Reprint requests to Fabio Sabogal, PhD, California Medical Review, Inc, One Sansome St, Suite 600, San Francisco, CA 94104 (e-mail: capro.fsabogal@sdps.org).

TABLE 1.—*Percentage of Distribution and Percentage of Mammography Screening in 1992 (Annual) and 1993 or 1994 (Biennial)*

Race and Age	Distribution, % n = 845,442	Mammography, % 1992	Mammography, % 1993 or 1994
All*	100.0	28.8	39.9
Race			
Black	4.8	19.2	29.7
White	88.0	30.1	41.3
Age, y*			
65 to 69	29.3	35.4	50.3
70 to 74	26.4	33.5	46.9
75 to 79	20.3	28.3	38.8
80 to 84	13.5	20.4	27.2
≥85	10.5	9.8	11.8

*Includes races other than black or white.

than black or white is considered unreliable.[12] In addition to reporting the mean age of these women, we categorized age into five-year intervals to ease some presentations.

We used Mantel-Haenszel methods[13] to estimate the association between later and earlier screening mammography, adjusted for age and race.

Results

Within this study group, about 29% had a mammogram in 1992 (Table 1). There were statistically significant differences, however, in screening within age and race categories. For example, fewer black women than white women had mammograms, and fewer older women than younger women had mammograms.

Although the mean age of these women was 74.6 years in 1992, women who had a mammogram in 1992 were younger (72.6 years) than women who did not have a mammogram (75.4 years). Despite racial differences in mammography use, the mean age of black women (74.5 years) was similar to that of white women (74.7 years). Furthermore, although black women and white women who had a mammogram in 1992 were close in age (72.8 and 72.6 years, respectively), black women who did not have a mammogram in 1992 were younger (74.9 years) than their white counterparts (75.6 years).

About 10% more women were screened during the subsequent two-year period, 1993 to 1994 (39.9%); however, the relationships between screening and the covariates age and race were similar for both annual and biennial screening (Table 1).

Of the women with earlier screening, more than 70% had subsequent screening (Table 2). Of women without a mammogram in 1992, however, only 27.4% had a later mammogram. When adjusted for race and age, women with a 1992 mammogram were 2.3 times more likely to have another screening mammogram in 1993 or 1994 than women without the 1992 mammogram. Adjustment led to similar estimates among stratified age groups, but not race groups. This result indicates that age, but not race, affects the relationship between earlier and later screening.

Although the overall mammography rates decrease with age, the importance of the earlier mammogram in predicting later mammograms increases. Among the younger women, those with an earlier mammogram were about twice as likely to have a later mammogram than those without the earlier mammogram; whereas among the oldest age group, women with an early mammogram were nearly six times as likely to have a later mammogram. The effects of earlier screening on later screening was slightly stronger among black women than among white women, despite their overall lower mammography use.

Discussion

This study provides recent information about subsequent screening mammography among a large number of

TABLE 2.—*Relative Risks for Mammography Screening in 1993 or 1994 by Mammography Screening in 1992*

Age and Race	Mammography in 1993 or 1994, % Mammogram in 1992	Mammography in 1993 or 1994, % No Mammogram in 1992	Relative Risk (95% Confidence Interval) Unadjusted	Relative Risk (95% Confidence Interval) Adjusted*
All†	70.8	27.4	2.58 (2.57–2.59)	2.27 (2.26–2.28)
Race				
Black	61.7	22.1	2.79 (2.71–2.87)	2.60 (2.52–2.67)
White	71.5	28.3	2.53 (2.51–2.54)	2.25 (2.23–2.26)
Age, y†				
65 to 69	75.3	36.7	2.05 (2.04–2.07)	2.02 (2.00–2.03)
70 to 74	73.4	33.5	2.19 (2.17–2.21)	2.16 (2.14–2.18)
75 to 79	68.1	27.3	2.50 (2.47–2.52)	2.46 (2.43–2.49)
80 to 84	60.0	18.7	3.21 (3.14–3.27)	3.78 (3.12–3.23)
≥85	46.4	8.0	5.81 (5.62–6.02)	5.75 (5.59–6.95)

*All: adjusted for age and race; race: adjusted for age; age: adjusted for race.
†Includes races other than black and white.

Medicare beneficiaries. We demonstrated that beneficiaries with an earlier mammogram are more than twice as likely to have a later mammogram as beneficiaries without an earlier mammogram. This finding is strongest among older women and black women, groups with lower overall screening rates. We found a much higher rate of subsequent screening mammography among this population of Medicare women (about 70%) than in an earlier study of low-income women (in which 45% of women had subsequent screening mammograms).[9] Our finding, however, is consistent with results from Sherbourne and colleagues, who found mammography at the beginning of their study period to be the strongest predictor of mammography two years later.[11] This relationship has important implications for the long-term benefits of cancer screening programs; reducing barriers for women who have never been screened may promote long-term adherence to cancer screening guidelines.

We found the relationship between the earlier and later mammograms increased with age. Because morbidity increases with age, however, a possible explanation is that the same disabilities that prevent the index mammogram prevent subsequent mammograms.

One explanation for these results is the effects of the physician recommendation[14] on screening, which could explain, in part, these results; women with physicians who recommend the first mammogram may have the same physician recommending the later mammograms. On the other hand, it could be that one physician recommendation leads to long-term adherence to screening guidelines.

One limitation of Medicare claims data is the probable underestimate of mammography; beneficiaries with mammograms paid for by other sources—out-of-pocket, subsidized or free programs, or private insurance—are not included in our mammography count.[4] This undercount would make our finding appear stronger than the actual relationship. In addition, the effects of managed care enrollment on statewide estimates are unknown. We have no comparable information about screening mammography for women enrolled in a managed care program. Indeed, for both these reasons, it is more accurate to phrase our results in mammography bills: women with one Medicare-billed mammogram are more likely to have Medicare-billed mammograms in subsequent years than women without the first billed mammogram. As a corollary, the relatively high cost of a mammogram increases incentives to obtain Medicare coverage.

We show that efforts to increase mammography use may have long-term effects. Early screening mammography is an important predictor of later screening mammography. Further study of factors that affect this relationship would enable health educators to aim more effectively their efforts toward adherence to screening mammography. Nonetheless, this evidence fuels optimism that our short-term interventions may lead to long-term benefits for older women.

REFERENCES

1. Kerlikowske K, Grady D, Rubin S, Sandrock C, Ernster V. Efficacy of screening mammography: a meta-analysis. JAMA 1995; 273:149–154

2. US Preventive Services Task Force. Guide to Clinical Preventive Services. 2nd ed. Alexandria, Va, International Medical Publishing, 1996

3. Dodd GD. Screening for breast cancer. Cancer 1993; 72:1038–1042

4. Health Care Financing Administration. 1992–1993 Mammography Services Paid by Medicare: State and County Rates. Washington, DC, Health Care Financing Administration, 1995

5. Burns RB, McCarthy EP, Freund KM, et al. Variability in mammography use among older women. J Am Geriatr Soc 1996; 44:922–926

6. Parker JD, Gebretsadik T, Sabogal F, et al. Mammography screening among California Medicare beneficiaries: 1993–1994. Am J Prev Med 1998; 15:198–205

7. Blustein J. Medicare coverage, supplemental insurance, and the use of mammography by older women. N Engl J Med 1995; 332:1138–1143

8. Makuc D, Freid V, Parsons P. Health Insurance and Cancer Screening Among Women. Hyattsville, Md, National Center for Health Statistics, 1994. Advance Data From Vital and Health Statistics, No. 254

9. Song L, Fletcher R. Breast cancer rescreening in low-income women. Am J Prev Med 1998; 15:128–133

10. Lerman C, Rimer B, Trock B, Balsheim A, Engstrom P. Factors associated with repeat adherence to breast cancer screening. Prev Med 1990; 19:279–290

11. Sherbourne C, Hays R, Ordway L, DiMatteo M, Kravitz R. Antecedents of adherence to medical recommendations: results from the medical outcomes study. J Behav Med 1992; 15:447–468

12. Lauderdale DS, Goldberg J. The expanded racial and ethnic codes in the Medicare data files: their completeness of coverage and accuracy. Am J Public Health 1996; 86:712–716

13. Kleinbaum DG, Kupper LC, Morgenstern H. Epidemiologic Research. New York,NY, Van Nostrand Reinhold, 1982

14. Fox S, Murata P, Stein J. The impact of physician compliance on screening mammography for older women. Arch Intern Med 1991; 151:50–56

The analyses upon which this publication is based were performed under Contract number 500-96-P535, entitled, "Utilization and Quality Control Peer Review Organization for the State of California," sponsored by the Health Care Financing Administration (HCFA), Department of Health and Human Services. The content of this publication does not necessarily reflect the view or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the US Government. The author assumes full responsibility for the accuracy and completeness of the ideas presented. This article is a direct result of the Health Care Quality Improvement Program initiated by HCFA, which has encouraged identification of quality improvement projects derived from analysis of patterns of care, and therefore required no special funding on the part of this Contractor. Ideas and contributions to the author concerning experience in engaging with issues presented are welcomed.

Articles

Mental Illness in Elementary-School-Aged Children

ANAND CHABRA, MD, MPH; GILBERTO F. CHÁVEZ, MD, MPH; *and* EMILY S. HARRIS, MD; *Sacramento, California*

We conducted a retrospective analysis of 1992 hospital discharge data to determine the incidence of mental illness hospitalizations among elementary-school-aged children and to analyze differences in hospital use by selected population characteristics. We analyzed population-based records of hospitalizations of 6- to 12-year-olds (n = 4,460) with a principal diagnosis of mental illness and calculated relative risks (RRs) for hospitalization by sex, race/ethnicity, and payment source. Mental illnesses accounted for 8.1% of hospitalizations and 28.9% of hospital days for 6- to 12-year-olds. Hospital charges totaled $85 million. Boys had a higher risk of mental illness hospitalization than girls (RR 1.96; 95% confidence interval [CI] 1.84–2.08). Latino children had a lower risk than whites (RR 0.22; 95% CI 0.20–0.24), as did children in the "Asian/other" group (RR 0.12, 95% CI 0.10–0.15). Inpatient hospitalizations for mental illness have a major impact on hospital morbidity for elementary-school-age children. Boys are overrepresented and Latinos and Asians/others are underrepresented among mental illness hospitalizations. Clinical implications for these findings and barriers to the delivery of inpatient mental health care are discussed.

(Chabra A, Chávez GF, Harris ES. Mental illness in elementary-school-aged children. West J Med 170:28–34)

The mental health needs of children in the United States remain largely unmet or underserved.[1,2] Prevalence estimates in both industrialized and developing countries suggest that as many as 14% to 20% of children and teenagers meet criteria for one or more mental health disorders,[3,4] findings that hold true for young people in the United States.[3] According to utilization data, only 20% to 40% of US children and teenagers receive the inpatient or outpatient mental health services they require.[2,5] In this article, we examine inpatient psychiatric hospitalization of elementary-school-age children (aged 6 to 12 years) in an effort to better understand the intensive services provided to this age group.

Inpatient hospitalization for the treatment of childhood mental illnesses is generally limited to children who are unsafe or acutely disturbed, who require skilled observation and assessment throughout the day, or who need rapid intervention during crisis situations. Additional reasons for inpatient care include accessibility to general hospital services, controlled initiation of psychotropic medication, treatment for severe psychosomatic disorders, and links with outpatient services.[6] One review of hospital admissions from the late 1970s and early 1980s showed that hospitalized children had a high incidence of a history of assaultive and suicidal behavior, poor academic performance, noncompliant behavior, organic involvement, and multiple family disruptions and separations.[7] Another review noted that in most studies boys hospitalized for mental illness outnumbered girls and that common primary diagnoses for those hospitalizations included the spectrum of behavior disorders (e.g., attention-deficit disorder, adjustment disorder, conduct disorder) and emotional disorders (e.g., major depression, dysthymia).[8] Many of these children are followed by multiple community agencies, and many are the victims of neglect or abuse.[6] Previous studies of the hospitalization of children for mental illness have focused on the use of general hospitals for child psychiatric inpatient treatment,[9,10] length of stay,[11–18] and the effect of insurance benefits on hospital use.[19,20]

Limited data, however, are available on race and ethnic differences in hospitalization rates for children. Two studies found that 72% to 82% of psychiatric hospitalizations were for whites.[20,21] One of the studies found no difference between blacks and whites or between Hispanic/other groups and whites in the probability of children using inpatient services for child psychiatric

From the California Department of Health Services (Drs Chabra and Chávez), Maternal and Child Health Branch, Sacramento, California; the Pregnancy and Infant Health Branch (Dr Chávez), Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia; and the Division of Child, Adolescent and Family Psychiatry (Dr Harris), Department of Psychiatry, University of California at Davis, Sacramento, California.

Reprint requests to Dr. Chabra, California Department of Health Services, Maternal and Child Health Branch, 2151 Berkeley Way, Annex 4, Room 200, Berkeley, CA 94704-1011 (e-mail: achabra@hw1.cahwnet.gov).

This research was supported by funds from the California Department of Health Services, Maternal and Child Health Branch.

disorders.[20] Our literature review did not uncover any population-based data addressing racial and ethnic differences in hospitalizations for mental illness among children of elementary school age.

We conducted this population-based descriptive epidemiologic study to evaluate recent patterns of hospitalization for mental illness among young school-age children in California. We were interested in identifying the psychiatric diagnoses resulting in hospitalization, the racial/ethnic and sex differences in the relative risk (RR) for hospitalization, and the financial effect of the hospitalizations on the health care delivery system.

Methods

We obtained data on all hospital discharges from nonfederal, acute care hospitals in California during 1992 from the California Office of Statewide Health Planning and Development. Records were selected for all patients aged 6 to 12 years with a principal discharge diagnosis of mental illness according to *International Classification of Diseases, 9th Revision, Clinical Modification* (*ICD-9-CM*) codes 290 through 319. We identified 4,460 hospital discharges that met our selection criteria.

The 11 state hospitals operated by the Department of Developmental Services and the Department of Mental Health, which serve the more severely mentally disordered and developmentally disabled clients, are not represented in the above data, so we obtained data on hospitalizations for 6- to 12-year-olds from those institutions to create a more complete picture of childhood mental illness hospitalizations. The Department of Mental Health reported a total of 19 children aged 6 to 12 years discharged in 1992, and the Department of Developmental Services reported a total of 32 children aged 6 to 12 years.

For our study, we reclassified *ICD-9-CM* codes into broader diagnostic categories, primarily by using criteria from the *Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised* (*DSM-III-R*).[22] Each of the seven diagnostic categories—depressive, disruptive behavior, anxiety, adjustment, psychotic, impulse control, and bipolar disorders—contained ≥100 cases and together accounted for 89.5% of mental illness diagnoses. The remaining *ICD-9-CM* codes were analyzed separately.

We divided race into four racial/ethnic groups and coded each group: white, African American, Latino (Hispanic), and Asian/other (Native American/Eskimo, Asian, other). We also divided the expected payment source into four groups and coded each group: fee-for-service (self-pay and private insurance), Medi-Cal (Medicaid), health maintenance organizations (HMO) and prepaid health plans (PHP), and other (e.g., Civilian Health and Medical Program of the Uniformed Services, Short-Doyle funds). We followed guidelines of the Office of Statewide Health Planning and Development and coded patients receiving services through an HMO/PHP but covered by Medi-Cal as Medi-Cal. Because Kaiser Permanente Hospitals and Shriners Children's Hospitals are exempted by the state guidelines from reporting hospital charges, we excluded cases from those institutions (n = 43) from analyses of mean and total hospital charges. For hospitalizations of more than 365 days (n = 3), total hospital charges covered only the last 365 days.[23]

Data on the subset of hospital discharges containing unique identifiers were analyzed to compare children with one hospitalization for mental illness in 1992 and those with more than one hospitalization for mental illness in that year. Percentages by race/ethnicity and sex were calculated for 1,932 children with one mental illness hospitalization in 1992 and for 350 children with multiple mental illness hospitalizations. (The records of 33 children were not included in the latter calculation because they contained inconsistencies in sex or racial/ethnic coding across hospitalizations.) Of these 350 children, we further analyzed the diagnoses of the 285 children with two hospitalizations for mental illness in 1992.

We calculated hospitalization rates and RRs by using population numbers obtained from the 1992 intercensal projections for the population aged 6 to 12 years (from the State of California Department of Finance). Estimates for the population of children eligible for Medi-Cal used to calculate the RRs by payment source were obtained from the Medical Care Statistics Section of the Fiscal Forecasting and Data Management Branch, California Department of Health Services. Race-/ethnic, payment source–, and sex-specific RRs for hospitalization were estimated with a 95% confidence interval (CI). We used SPSS for Windows,[24] SAS,[25] and Epi Info[26] for data analysis.

An additional analysis was conducted using 1996 hospital discharge data to ascertain if major changes in hospital utilization for mental illness in the elementary-school-age population occurred between 1992 and 1996. We identified 4,878 hospital discharges that met our selection criteria. Rates were calculated using the 1996 intercensal projection for the population aged 6 to 12 years. Ethnicity and race were coded separately in 1996 hospital discharge data. To make 1992 and 1996 data comparable, all children of Hispanic ethnicity were coded as Latino. Children of non-Hispanic or unknown ethnicity were coded based on race: white, African-American, and Asian/other (Native American/Eskimo/Aleut, Asian/Pacific Islander, other). Those whose race (n = 55) and sex (n = 2) were unknown were not included in the rates and RRs by sex and racial/ethnic group.

Results

In 1992 in California, 4,460 (8.1%) of the 54,827 hospital discharges of children aged 6 to 12 years were for a primary diagnosis of mental illness. Most of these discharges (>85%) were from psychiatric hospitals. These 4,460 hospitalizations accounted for more than $85 million in hospital charges and 89,916 days of hospitalization. The hospital stay (mean ± SD) was 20.2 ± 23.8 days, and the hospital charge per stay was $19,334 ± $17,613. The discharge rate for cases of mental illness

TABLE 1.—*Demographic Characteristics of Hospitalizations for Mental Illness in Children of Elementary-School Age, California, 1992*

Characteristic	No. (%)*
n	4,460
Age (y)	
6–8	1,025 (23.0)
9–10	1,185 (26.6)
11–12	2,250 (50.4)
Sex	
Female	1,460 (32.7)
Male	3,000 (67.3)
Race/Ethnicity	
White	3,232 (72.5)
African American	556 (12.5)
Latino	560 (12.6)
Asian	55 (1.2)
Other	26 (0.6)
Native American	14 (0.3)
Unknown	17 (0.4)
Expected payment source	
Medi-Cal	1,882 (42.2)
Fee for service	1,127 (25.3)
HMO/PHP	900 (20.2)
Other	550 (12.3)

*Some totals do not add up to 100.0% due to rounding of percentages. One case is missing a payment source.

alone was 1.4 per 1,000 children aged 6 to 12 years. Mental illness accounted for 14.7% of all hospital charges and 28.9% of all hospital days in this group.

The seven major diagnostic categories accounted for 3,991 hospitalizations, with depressive disorders alone accounting for 2,356 hospitalizations (52.8% of the total). Fifteen diagnoses accounted for 368 of the 469 remaining hospitalizations, among them anxiety disorders of childhood or adolescence (n = 55); postconcussion syndrome (n = 52); other disorders of infancy, childhood, or adolescence (n = 44); substance abuse disorders (n = 28); pervasive developmental disorders (n = 28); eating disorders (n = 27); and unspecified impulse control disorders (n = 23). Additional categories included other specified organic brain syndromes (chronic, n = 20), somatoform disorders (n = 17), organic affective syndrome (n = 16), schizophrenia (n = 14), organic personality syndrome (n = 13), tic disorders (n = 12), dissociative disorders (n = 11), and mental retardation (n = 8).

Boys accounted for more than two-thirds of the hospitalizations, and white children accounted for almost three-fourths (Table 1). Medi-Cal was the largest single payment source; fee-for-service and HMO/PHP combined covered a somewhat higher percentage of hospital stays. More than half of the hospitalizations were for children aged 11 to 12 years.

Data (not shown) were obtained from the 2,781 cases (62%) containing unique identifiers—encrypted social security numbers that are unique to each patient but cannot be followed back to actual social security numbers. These identifiers allowed hospitalizations for a single child to be linked across time. Of children with unique identifiers, 83.5% experienced one, 13.3% experienced two, and 3.2% experienced three or more hospitalizations for mental illness in 1992. The cohort of children with one mental illness hospitalization in 1992 was 68.1% male, 71.5% white, 12.7% African American, 13.0% Latino, 2.4% Asian/other, and 0.4% race unknown. Children with multiple hospitalizations in 1992 were 69.7% male, 73.1% white, 15.4% African American, 10.3% Latino, and 1.1% Asian/other.

Of the 285 children with two hospitalizations for mental illness in 1992, 260 had principal diagnoses that fit into the seven major diagnostic categories. For the majority (63.8%) of those 260 children, diagnostic categories were consistent for the two admissions. Specifically, 103 children were hospitalized twice for depressive disorders, 28 children twice for disruptive behavior disorders, 11 children twice for anxiety disorders, 7 children twice for adjustment disorder, 7 children twice for psychotic disorders, 6 children twice for impulse control disorders, and 4 children twice for bipolar disorders. The remaining 94 children (36.2%) had diagnoses falling into two different diagnostic categories on the two occasions.

The RR of hospitalization for mental illness was significantly higher for boys than girls (RR 1.96; 95% CI 1.84–2.08). The RRs for each diagnostic group are presented in Table 2. The highest RRs for boys were for impulse control and disruptive behavior disorders. Bipolar, psychotic, depressive, and anxiety disorders had smaller elevations in the risk of hospitalization for boys compared with girls. No sex difference was found in the RR of hospitalization for adjustment disorder.

We found significant differences in the RR of hospitalization for mental illness among racial/ethnic groups (Table 3). RRs for all psychiatric diagnoses were significantly lower for the Latino and Asian/other groups than for whites. Our data combine Asian children with other groups to create a population-based estimate as reflected in Tables 3 and 4; however, census data reveal that the vast majority of the Asian/other group are, in fact, Asian. We calculated a proportional hospitalization ratio for mental illness ([observed hospitalizations/expected hospitalizations] × 100) for hospitalized Asians alone compared with hospitalized whites aged 6–12 years and found that Asians had a ratio of 14.6%, which is consistent with the RR for the Asian/other group. This suggests that our findings are consistent with a decreased risk of hospitalization for mental illness among Asian children, although data on Asian/other children combined may overestimate the risk related to Asian children alone. The overall risk of mental illness hospitalization for African-American children was not significantly different from that for white children.

After we stratified the data by Medi-Cal payment status (Table 4), the RR of hospitalization for mental illness for

TABLE 2.—*Relative Risk of Hospitalization for Mental Illness by Diagnosis and Sex, Children Aged 6 to 12 years, California, 1992*

Diagnosis and Sex	*No. Hospitalizations*	*Hospitalization Rate (per 1,000 Population)*	*RR*	*95% CI*
All mental illness diagnoses				
Female	1460	0.9	1.00	
Male	3000	1.8	1.96	1.84–2.08
Depressive disorders				
Female	840	0.5	1.00	
Male	1,516	0.9	1.72	1.58–1.87
Disruptive behavior disorders				
Female	116	0.1	1.00	
Male	591	0.4	4.85	3.98–5.92
Anxiety disorders				
Female	120	0.1	1.00	
Male	163	0.1	1.29	1.02–1.64
Adjustment disorder				
Female	113	0.1	1.00	
Male	125	0.1	1.05	0.82–1.36
Psychotic disorders				
Female	52	0.0	1.00	
Male	117	0.1	2.14	1.55–2.97
Impulse control disorders				
Female	20	0.0	1.00	
Male	110	0.1	5.24	3.25–8.43
Bipolar disorders				
Female	33	0.0	1.00	
Male	75	0.0	2.16	1.44–3.26

the Latino and Asian/other groups remained significantly lower than the risk for whites in both Medi-Cal and non–Medi-Cal payment categories. For African-American children, however, the risk was approximately half that for whites in the Medi-Cal payment category but 28% greater in the non–Medi-Cal payment category.

Our additional analysis of 1996 hospitalization data for children aged 6 to 12 years (not shown) revealed 4,878 hospitalizations for mental illness for a rate of 1.4 hospitalizations per 1,000 population. The hospitalization rate for boys was 1.8 per 1,000, and the rate for girls was 1.0 per 1,000 (RR 1.82; 95% CI 1.72–1.93). The hospitalization rates by race/ethnicity were 1.98 per 1,000 for whites, 3.45 per 1,000 for African Americans, 0.49 per 1,000 for Latinos, and 0.55 per 1,000 for Asians/others. When compared with white children, African-American children had a higher RR of hospitalization for mental illness (RR 1.74; 95% CI 1.62–1.87), while Latino (RR 0.25; 95% CI 0.23–0.27) and Asian/other (RR 0.28; 95% CI 0.24–0.32) children had lower RRs for these hospitalizations. The seven diagnostic categories accounted for 86.6% of the hospitalizations; 43.4% of the hospitalizations were for depressive disorders.

Discussion

Mental illnesses accounted for 8.1% of hospitalizations among elementary-school-age children (aged 6–12) in California in 1992. While children in this age group experience relatively few acute hospitalizations compared with other age groups, the ones who are hospitalized are often treated for mental illness. The mean length of stay for mental illness hospitalizations is long, and the mean charges per hospitalization are high. As a result, these hospitalizations accounted for more than one-fourth of all hospital days in this age group and one-seventh of all hospital charges. Moreover, more than one-half of the total cost was paid by the public sector, amounting to more than $46 million. Given the high cost of inpatient treatment for mental illness, early intervention, primary and secondary prevention, and the development of alternative levels of care would significantly decrease the financial burden of care for this age group. Further study of the utilization patterns for intensive mental health services by this younger age group are needed.

In our study, elementary-school-age boys were more likely than girls to be hospitalized for a mental illness. This finding is not surprising; behavior disturbances accounted for almost 20% of the hospitalizations and are three or four times more prevalent among boys than girls in this age group.[22] Depressive disorders accounted for one-half of the total hospitalizations, and almost two-thirds of those admissions were for boys (RR 1.72; 95% CI 1.58–1.87). Our expectation is that the risk for depression is the same for both sexes before puberty. The predominance of boys may reflect the greater likelihood of comorbid behavioral

TABLE 3.—*Relative Risk of Hospitalization for Mental Illness by Diagnosis and Race/Ethnicity, Children Aged 6 to 12 years, California, 1992**

Diagnosis and Race/Ethnicity	*No. Hospitalizations*	*Hospitalization Rate (per 1000 Population)*	*RR*	*95% CI*
All mental illness diagnoses				
White	3,232	2.23	1.00	
African American	556	2.20	0.99	0.90–1.08
Latino	560	0.50	0.22	0.20–0.24
Asian/other	95	0.27	0.12	0.10–0.15
Depressive disorders				
White	1,733	1.19	1.00	
African American	268	1.06	0.89	0.78–1.01
Latino	309	0.27	0.23	0.20–0.26
Asian/other	39	0.11	0.09	0.07–0.13
Disruptive behavior disorders				
White	515	0.35	1.00	
African American	103	0.41	1.15	0.93–1.42
Latino	80	0.07	0.20	0.16–0.25
Asian/other	7	0.02	0.06	0.03–0.12
Anxiety disorders				
White	222	0.15	1.00	
African American	34	0.13	0.88	0.61–1.26
Latino	21	0.02	0.12	0.08–0.19
Asian/other	5	0.01	0.09	0.04–0.23
Adjustment disorder				
White	162	0.11	1.00	
African American	37	0.15	1.31	0.92–1.88
Latino	26	0.02	0.21	0.14–0.31
Asian/other	12	0.03	0.31	0.17–0.55
Psychotic disorders				
White	98	0.07	1.00	
African American	30	0.12	1.76	1.17–2.65
Latino	32	0.03	0.42	0.28–0.63
Asian/other	6	0.02	0.26	0.11–0.58
Impulse control disorders				
White	96	0.07	1.00	
African American	21	0.08	1.26	0.78–2.02
Latino	8	0.01	0.11	0.05–0.22
Asian/other	3	0.01	0.13	0.04–0.41
Bipolar disorders				
White	91	0.06	1.00	
African American	9	0.04	0.57	0.29–1.13
Latino	6	0.01	0.08	0.04–0.19
Asian/other	2	0.01	0.09	0.02–0.37

*Seventeen cases with unknown racial/ethnic group are not included in this table.

disorders and more lethal suicidal ideation and attempts in boys; girls may cause fewer disruptions.

The differences we found in hospital rates for selected racial/ethnic groups are, perhaps, the most important findings of the study. Few data are available on the risk or prevalence of mental disorders or the utilization of mental health services by minority elementary-school-age children. Both Latino and Asian children had a much lower risk of hospitalization for mental illness disorders than white or African-American children. This finding is consistent with reports of underutilization of inpatient mental health care by Latino and Asian minority adult population groups.[27,28] Lower prevalence rates of severe psychopathology in Asian and Latino child populations may be one explanation for lower rates of care use; alternatively, factors related to race, cultural background, and socioeconomic status, including real or perceived institutional, cultural, language, or economic barriers, may contribute to different rates of care use.[28] Based on our data regarding economic factors, utilization rates for Latino and Asian children were unrelated to source of payment (Medi-Cal versus non–Medi-Cal).

TABLE 4.—*Relative Risks of Hospitalization for Mental Illness by Medi-Cal Status and Race/Ethnicity for Children Aged 6 to 12 Years, California, 1992**

	Medi-Cal (n = 1,873)	*Non–Medi-Cal† (n = 2,569)*
White	1.00	1.00
African American	0.45 (0.40–0.51)	1.28 (1.12–1.46)
Latino	0.16 (0.14–0.18)	0.21 (0.19–0.24)
Asian/other	0.07 (0.05–0.09)	0.16 (0.12–0.20)

*Data are RR (95% CI). Eighteen cases are not included, 17 of unknown racial/ethnic group and one missing a payment source.

†Includes payment sources such as Short-Doyle funds, HMO/PHPs, private insurance, and Civilian Health and Medical Program of the Uniformed Services.

In contrast, overall rates of hospitalization for mental illness within the child population of African Americans did not differ from rates of hospitalization for white children. For African Americans, however, relative rates of use of inpatient hospitalization for mental illness depended on the source of payment. Among children using Medi-Cal, rates for African Americans were lower than for white children; in contrast, the RR was greater for African Americans than for whites among those using other payment sources (which combines diverse payment sources). Higher differential admission rates for African Americans were also identified as a trend in adult use of mental health services and raise concerns regarding misdiagnosis or overdiagnosis resulting from cultural or language barriers, increased incidence of severe family problems including substance or alcohol abuse, and declining or absent mental health resources in the community.[27] Evidence from adult studies does not suggest that minority status is related to prevalence rates of severe mental illness, although epidemiological study of child mental health disorders and service use is needed to clarify these issues in the younger population.

Some have argued that minority adolescents disproportionately receive their mental health services from nonmedical sources, including the welfare and juvenile justice systems.[29,30] The same may be true for the younger population studied here. The bias toward correctional institutions instead of psychiatric care for violent adolescents has been noted among African-American youth,[30] as has the disproportionate share of institutional placements (foster homes, residential homes, and welfare placements) among African-American, American Indian, and Hispanic youth compared with whites.[31] In addition, the low rates of psychiatric hospitalization among Asian children may be associated with increases in hospitalizations for other somatic disorders, although we did not find this to be the case in a previous study of elementary-school-age children.[32] While it appears that no single factor explains the racial/ethnic variations in pediatric hospitalization for mental illness, care must be taken to ensure that minority children are not relegated to a lower level of psychiatric care or placement than white children.

There are several limitations to our study that deserve mention; several are inherent in using hospital discharge data. First, the unit of analysis for our study is hospitalizations rather than hospitalized individuals because more than one-third of the records had no unique identifier. Nonetheless, a review of the remaining records demonstrated that more than 80% of children were hospitalized only once. In addition, the patterns of sex and racial/ethnic breakdowns for children with unique identifiers (either with single or multiple hospitalizations) were similar to those related to all cases, further supporting our use of hospitalization data to look at population risks. Second, our data contain only hospital charges and do not include physician charges; our estimates of the cost related to inpatient mental health treatment are therefore conservative. Third, the data in this study address only the first (principal) diagnosis; it is evident from numerous studies that mental disorders in children are highly comorbid. Diagnostic categories based on the first diagnosis alone do not fully describe the complexity of cases with multiple mental illness diagnoses or with a combination of medical and psychiatric diagnoses.

Finally, these data from 1992 are aging and may not reflect changes in the health care system under managed care. As a result, we also analyzed data for the same population using 1996 hospital discharge data, the most recent available. We found a constant rate of 1.4 hospitalizations for mental illness among elementary-school-age children per 1,000 population in both 1992 and 1996. Almost half of those hospitalizations were for depressive disorders. Sex-specific rates of hospitalization for mental illness were 1.8 per 1,000 for both years for boys, and 0.9 per 1,000 in 1992 and 1.0 per 1,000 in 1996 for girls. Rates for the various racial/ethnic groups varied somewhat between 1992 and 1996 although, as in 1992, rates were again much lower for Latinos (0.49 per 1,000) and Asians/others (0.55 per 1,000) than for whites (1.98 per 1,000) in 1996. While rates for African Americans were essentially the same as for whites in 1992, in 1996 African-American children had a hospitalization rate of 3.45 per 1,000, a rate significantly higher than the rate for white children. It is unclear what role changes in the coding of race and ethnicity in 1996 hospital data had on these race-/ethnicity-specific hospitalization rates. Nonetheless, data from 1996 confirm that hospitalizations for mental illness continue to be a significant problem in the elementary-school-age population with the changes under managed care, and that sex-specific and race-/ethnicity-specific variations are still present, and, in the case of African Americans, may be increasing.

The reliance on hospital discharge data is a strength of this study given the importance of this type of data in studies of hospital utilization.[33,34] In addition, periodic studies by the California Office of Statewide Health Planning and Development to maintain the quality of collected data suggest that the error rates for the variables of interest in this study (race and principal diagnosis) are acceptable.[35] A second strength is our use of population-based data from the largest US state, providing a sample large enough to look at illness categories across sex and racial/ethnic groups. In addition, the use

of population-based data eliminates many of the biases associated with data limited to select populations. Hospital discharge data for this study accurately reflect the hospital morbidity related to mental illness for the age group of interest for the entire state.

Health care practitioners should be aware of the impact of mental illness and mental illness hospitalization among preteen children. While these children are rarely hospitalized, their hospitalizations are often for psychiatric conditions, particularly depression. As managed health care systems continue to expand, it is vital that the mental health needs of these children are addressed through both outpatient and inpatient mental health benefits. In addition, providers and health care agencies should address these concerns through prevention programs and targeted interventions for high-risk children.

These findings also suggest that clinicians need to pay special attention to mental health issues among minority elementary-school-aged children. Patients from minority groups (particularly Latino and Asian populations) are less likely to use inpatient services for psychiatric conditions than white children but may still have the same prevalence of psychiatric conditions as white children. Consequently, minority children who need mental health services but whose families are reluctant to use psychiatric hospitalization may need to be referred to outpatient or nonmedical services that they find more acceptable. Nonmedical sources of mental health care may include schools, religious organizations, families, community organizations, and government agencies.

In summary, this population-based study shows clear disparities by race/ethnicity and sex in hospitalization for mental illness among elementary-school-age children. Not surprisingly, boys are more likely to be hospitalized than girls; however, the significant underutilization of services among Latino and Asian children and higher rates of inpatient mental health care for a population of African Americans are cause for concern. We must gain an understanding of these disparities and take steps to ensure that minority children have access to appropriate mental health services. Further research on mental health services for children of racial/ethnic minorities is needed to better understand the social, economic, behavioral, and epidemiological determinants of care. In addition, a number of steps may improve the delivery of services to these children, including the development of more responsive service delivery systems, education for the mental health community regarding cultural issues, and the training and availability of minority mental health professionals.

REFERENCES

1. Saxe L, Cross T, Silverman N. Children's mental health: the gap between what we know and what we do. Am Psychol 1988; 43:800–807

2. Tuma JM. Mental health services for children: the state of the art. Am Psychol 1989; 44:188–199

3. Brandenburg NA, Friedman RM, Silver SE. The epidemiology of childhood psychiatric disorders: prevalence findings from recent studies. J Am Acad Child Adolesc Psychiatry 1990; 29:76–83

4. Giel R, de Arango MV, Climent CE, et al. Childhood mental disorders in primary health care: results of observations in four developing countries. Pediatrics 1981; 68:677–683

5. Realmuto GM, Bernstein GA, Maglothin MA, Pandey RS. Patterns of utilization of outpatient mental health services by children and adolescents. Hosp Community Psychiatry 1992; 43:1218–1223

6. Jemerin JM, Philips I. Changes in inpatient child psychiatry: consequences and recommendations. J Am Acad Child Adolesc Psychiatry 1988; 27:397–403

7. Cornsweet C. A review of research on hospital treatment of children and adolescents. Bull Menninger Clin 1990; 54:64–77

8. Scahill L, Riddle MA. Psychiatrically hospitalized children: a critical review. Yale J Biol Med 1990; 63:301–312

9. Kiesler CA, Simpkins C. Changes in psychiatric inpatient treatment of children and youth in general hospitals: 1980–1985. Hosp Community Psychiatry 1991; 42:601–604

10. Kiesler CA, Simpkins C, Morton T. The psychiatric inpatient treatment of children and youth in general hospitals. Am J Community Psychol 1989; 17:821–830

11. Shafii M, McCue A, Ice JF, Schwab JJ. The development of an acute short-term inpatient child psychiatric setting: a pediatric-psychiatric model. Am J Psychiatry 1979; 136:427–429

12. Sarles RM, Alessi N. Resolved: two-week psychiatric hospitalizations of children and adolescents are useless. J Am Acad Child Adolesc Psychiatry 1993; 32:215–220

13. Mossman D, Songer DA, Baker DG. Predicting length of children's psychiatric hospitalizations: an "ecologic" approach. Qual Rev Bull 1991; 17:269–274

14. Perry R, Karp JG, Padron-Gayol M, et al. Variables associated with length of psychiatric hospitalization of children during the 1980s. Hosp Community Psychiatry 1992; 43:390–391

15. Margolis LH, Petti RD. An analysis of the costs and benefits of two strategies to decrease length of stay in children's psychiatric hospitals. Health Serv Res 1994; 29:155–167

16. Christ AE, Tsemberis S, Andrews H. Childhood disorder DRG: consideration for a predictive model. J Am Acad Child Adolesc Psychiatry 1989; 28:47–52

17. Livingston R, Taylor JL, Crawford SL. Factors related to length of hospitalization of children with mental disorders. Hosp Community Psychiatry 1990; 41:193–195

18. Dalton R, Bolding DD, Woods J, Daruna JH. Short-term psychiatric hospitalization of children. Hosp Community Psychiatry 1987; 38:973–976

19. Liptzin B, Regier DA, Goldberg ID. Utilization of health and mental health services in a large insured population. Am J Psychiatry 1980; 137:553–558

20. Patrick C, Padgett DK, Burns BJ, Schlesinger HJ, Cohen J. Use of inpatient services by a national population: do benefits make a difference? J Am Acad Child Adolesc Psychiatry 1993; 32:144–152

21. Wallen J, Pincus HA. Care of children with psychiatric disorders at community hospitals. Hosp Community Psychiatry 1988; 39:167–172

22. Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised. Washington, DC, American Psychiatric Association, 1987

23. 1992 Discharge Data Tape Format Documentation. Sacramento, CA, Office of Statewide Health Planning and Development, State of California, 1993

24. SPSS for Windows. Base System User's Guide, Release 7.0. Chicago, IL, SPSS, 1996

25. SAS User's Guide. Basics, Release 6.03. Cary, NC, SAS Institute, 1988

26. Epi Info, Version 6: a Word-Processing, Database, and Statistics Program for Public Health on IBM-Compatible Microcomputers. Atlanta, GA, Centers for Disease Control and Prevention, 1994

27. Cheung FK, Snowden LR. Community mental health and ethnic minority populations. Community Ment Health J 1990; 26:277–291

28. Cheung FK. The use of mental health services by ethnic minorities. In Myers HF, Wohlford P, Guzman LP, Echemendia RJ (Eds): Ethnic Minority Perspectives on Clinical Training and Services in Psychology. Washington, DC, American Psychological Association, 1991, pp 23–31

29. Mason MA, Gibbs JT. Patterns of adolescent psychiatric hospitalization: implications for social policy. Am J Orthopsychiatry 1992; 62:447–457

30. Lewis DO, Shanok SS, Cohen RJ, Kligfeld M, Frisone G. Race bias in the diagnosis and disposition of violent adolescents. Am J Psychiatry 1980; 137:1211–1216

31. Stehno SM. Differential treatment of minority children in service systems. Soc Work 1982; 27:39–46

32. Chabra A, Chavez GF, Taylor D. Hospital use by pediatric patients: implications for change. Am J Prev Med 1997; 13(Suppl 2):30–37

33. Bindman AB, Grumbach K, Osmond D, et al. Preventable hospitalizations and access to health care. JAMA 1995; 274:305–311

34. Braveman PA, Egerter S, Bennett T, Showstack J. Differences in hospital resource allocation among sick newborns according to insurance coverage. JAMA 1991; 266:3300–3308

35. Meux EF, Stith SA, Zach A. Report of results from the OSHPD reabstracting project: an evaluation of the reliability of selected patient discharge data July through December 1988. Sacramento, CA, Office of Statewide Health Planning and Development, State of California, 1990

Internal Medical Residents' Ability to Diagnose and Characterize Major Depression

MITCHELL A. MEDOW, MD, PhD; STEVEN J. BOROWSKY, MD, MPH; SIGNE DYSKEN, MD; STEVE D. HILLSON, MD, MPH; SHARON WOODS, MD; *and* TIMOTHY J. WILT, MD, MPH; *Minneapolis, Minnesota*

The purpose of this study was to assess medical residents' knowledge of symptom criteria and subtypes of major depressive episode and their accuracy in diagnosing major depressive disorders and classifying episode severity and subtype according to criteria of the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*. Thirty-five third-year internal medicine residents completed a self-administered, written instrument containing 2 open-ended questions and 21 hypothetical scenarios. The sensitivity for recognizing major depressive disorder was 64%, and the specificity was 69%. The sensitivity for classifying severity was 86% for mild, 66% for moderate, 71% for severe, and 66% for severe with psychosis. Misclassification of severity was most commonly to a less severe class. For scenarios with a diagnosable subtype of a major depressive disorder, the sensitivity for classification was 34% for atypical, 51% for catatonic, 74% for melancholic, 100% for postpartum, and 94% for seasonal depression. When asked to enumerate the criteria symptoms for depression, 80% or more of the residents listed sad mood, loss of interest, weight change, and sleep disturbances; 14 to 21 (40%–60%) listed thoughts of death and worthlessness; other criteria were listed by 7 to 11 (20%–31%). When asked to list the episode subtypes, none was listed by more than 3 (9%) residents, although 13 (37%) residents volunteered psychotic as a subtype. Residents frequently failed to recognize the presence or absence of major depressive disorder and often misclassified episode severity and subtype on scenarios. Few could spontaneously list the episode subtypes. Methods must be developed to improve the recognition and classification of major depressive episodes to better direct treatment.

(Medow MA, Borowsky SJ, Dysken S, Hillson SD, Woods S, Wilt TJ. Internal medical residents' ability to diagnose and characterize major depression. West J Med 1999; 170:35–40)

The ability to recognize, diagnose, and treat major depressive disorder (MDD) is among the growing number of clinical competencies expected of primary care physicians. Previous studies have shown that primary care physicians often incorrectly conclude that depression is present when it is not and fail to identify patients who have the disease.[1–12] Moreover, when generalist physicians do diagnose depression, they do not effectively treat the disease,[8,13–19] using incorrect medications, inadequate dosages, and insufficient treatment duration. Although it is apparent that depression is often not properly diagnosed in primary care settings, the factors underlying this problem are less clear. Possible explanations include physicians' failure to consider the possibility of depression as the cause of the observed symptoms, inadequate knowledge of either the diagnostic criteria for depression or the proper treatment for the condition, a reluctance to manage mental health illnesses, or institutional and procedural barriers to treatment.

Clinical guidelines represent one strategy to overcome gaps in clinicians' knowledge about depression. Guidelines of the Agency for Health Care Policy and Research (AHCPR) for the diagnosis and treatment of depression[20,21] emphasize that the disorder is diagnosed by history, based on the nine criteria symptoms for a major depressive episode (MDE). Once the diagnosis is reached, specific treatment choices depend on the episode's severity (mild, moderate, severe without psychosis, or severe with psychosis) and specific subtype when applicable (atypical, catatonic, melancholic, seasonal, or postpartum), as well as concurrent conditions, current medications, and the patient's response to previous treatment. For example, a mild episode, according to the guidelines, may warrant a limited course of clinical follow-up before any

From the Department of General Internal Medicine, Minneapolis Veterans Affairs Medical Center (Dr Medow), Center for Chronic Disease Outcomes Research, Minneapolis Veterans Affairs Medical Center (Drs Borowsky and Wilt), Department of Psychiatry, Minneapolis Veterans Affairs Medical Center (Drs Dysken and Woods), and the Department of Internal Medicine, Hennepin County Medical Center (Dr Hillson), Minneapolis, Minn. Dr Medow is now with the Ohio State University College of Medicine and Public Health, Columbus, Ohio.

This study was supported in part by a fellowship (Dr Medow) from the Department of Veterans Affairs, Minneapolis, Minn.

Reprint requests to Mitchell A. Medow, MD, PhD, 4510 University Hospitals Clinic, 456 W 10th Ave, Columbus, OH 43210-1321.

ABBREVIATIONS USED IN TEXT

AHCPR = Agency for Health Care Policy and Research
DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition
MDD = major depressive disorder
MDE = major depressive episode

intervention is attempted, whereas moderate episodes should be treated pharmacologically. Optimal treatment also varies by subtype; for instance, atypical episodes respond better to monoamine oxidase inhibitors than to tricyclic antidepressants, whereas some catatonic episodes may require electroconvulsive therapy.

Therefore, the purpose of this study was to assess medical residents' knowledge of the diagnostic criteria used in the AHCPR depression guidelines, with a special focus on assessing severity and subtype of depressive episodes. This aspect has not been previously evaluated. The objectives of this study were to assess internal medical residents' knowledge of the criteria symptoms and subtypes of MDE and to use validated clinical scenarios to evaluate internal medicine residents' ability to diagnose MDD and classify episode severity and subtype.

Subjects and Methods

Study Population

Third-year residents in the University of Minnesota School of Medicine's Internal Medicine Residency Program assigned to continuity clinics at the Minneapolis Veterans Affairs Medical Center were eligible for the study. Of 38 eligible residents, 35 participated, for a participation rate of 92%. Informed consent was obtained from all subjects before participation.

Definitions

Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (*DSM-IV*),[22] criteria for MDE are as follows:

- One of the two mandatory symptoms, sad mood or loss of interest, must be present;
- There must be a total of five symptoms among sad mood, loss of interest, sleep disturbance, weight change, psychomotor abnormalities, fatigue, feelings of worthlessness, concentration difficulties, and preoccupation with death;
- The symptoms must be present for at least two weeks and cause significant impairment in the patient's life (the impairment criterion was added to the *Diagnostic and Statistical Manual of Mental Disorders, Third Edition*, criteria);
- The symptoms are not caused by an underlying medical condition or a substance; and
- The symptoms do not meet the criteria for a mixed episode or a bereavement reaction.

A patient with MDE can be diagnosed with MDD if there is no evidence of bipolar disorder and the mood symptoms are not due to an underlying psychotic condition. Severity, in the *DSM-IV*, is based on a symptom count and the degree of impairment in a patient's life. The *DSM-IV* subtype definitions were used.

Scenario Development

We developed a set of clinical scenarios to assess residents' ability to diagnose and classify episodes of depression. The scenarios were designed to reflect the diagnosis of depression according to *DSM-IV* criteria. Generating the scenarios involved two steps: specifying clinical patterns derived from the diagnostic criteria and then constructing two specific scenarios to represent each of the clinical patterns. Clinical patterns specify symptom constellations that "rule in" or "rule out" the diagnoses of depression based on *DSM-IV* criteria. We abstracted clinical patterns from the *DSM-IV* definitions of MDE, MDD, episode severity, and episode subtype. For example, the absence of both mandatory symptoms (sad mood and loss of interest) in the presence of five or more total symptoms excludes the diagnoses of MDE. Figure 1 shows the clinical patterns we derived.

Symptoms were randomly selected to match the clinical patterns. Descriptions of the symptoms were taken from a validated screening instrument for depression, the Inventory to Diagnose Depression[23] or from the *DSM-IV*. Additional information was added to some of the scenarios to match the clinical patterns: specification of a recent death, duration of symptoms less than two weeks, season, postpartum condition, coexisting medical or psychiatric conditions, and current medications. For the scenarios missing both of the two mandatory symptoms, we explicitly stated that the patient denies any sad feelings or loss of interest in his or her normally joyful activities.

Sex, age (18–75 years old), and symptom duration (2–16 weeks) were added to the scenarios. "Red herrings" were also used, so that the mere presence of a specific situation would not necessarily signal the correct diagnosis. For example, we did not want the occurrence of a birth to always signal postpartum depression. The generated scenarios were then edited for readability and consistency. Figure 2 shows two examples of clinical patterns and their respective scenarios.

Validity of Scenarios and Solutions

To achieve content validity, scenarios were generated to the precise *DSM-IV* definitions using symptom descriptions from the Inventory to Diagnose Depression or the *DSM-IV*, as described earlier. The scenarios were then reviewed by two psychiatrists and further edited according to their recommendations, to ensure face validity. For example, elderly and male patients were restricted to having weight loss and not weight gain. Also, symptoms were adjusted to correspond with other psychiatric diagnoses (such as schizophrenia) and severity.

A "gold standard solution" for each scenario was developed as the consensus of two additional staff psychiatrists (S.D. and S.W.) explicitly instructed to independently answer the questions in adherence with the *DSM-IV*

Patterns Not Meeting Criteria for Major Depressive Episode (MDE)
Missing a mandatory symptom, ≥5 total symptoms
Insufficient number of symptoms
Insufficient duration of symptoms
Symptoms caused by a medical condition
Symptoms caused by a medication
Symptoms caused by substance abuse
Symptoms better accounted for by bereavement reaction

Patterns Meeting Criteria for MDE, But Not Meeting Criteria for Major Depressive Disorder (MDD)
Schizoaffective or schizophrenic disorder
Previous manic episode

Patterns Meeting Criteria for Major Depressive Disorder
Mild depression
Moderate depression
Severe without psychosis depression
Severe with psychosis depression
Atypical subtype
Catatonic subtype
Melancholic subtype
Postpartum subtype
Seasonal subtype

Figure 1.—These clinical patterns of depression are based on definitions of the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition.*[22]

criteria. Disagreements were resolved by reviewing the *DSM-IV* criteria. Scenarios for which there remained a difference of opinion were modified to remove the elements of contention. Agreement between the two psychiatrists on their initial evaluation of the scenarios was evaluated using Cohen's κ.[24] For the classification of episode severity, $\kappa = 0.67$, representing "substantial" agreement.[25] For the classification of episode subtype, $\kappa = 0.88$, showing "almost perfect" agreement. For the diagnosis of MDD, there was less agreement, $\kappa = 0.56$, indicating "moderate" agreement, in part because one of the psychiatrists answered all the questions with regard to MDE, and the other assessed MDD. Some of the cases were designed to represent instances of MDE and not of MDD (such as a patient with bipolar disorder), accounting for most of the discrepancies. Complete agreement was reached for all cases.

Study Instrument

Each study instrument included 2 open-ended questions, followed by 21 clinical scenarios with associated questions

Clinical Pattern
Missing a mandatory symptom for major depressive disorder, but >5 total criteria symptoms
Clinical Scenario
A 22-year-old man tells you that he frequently thinks of dying in passive ways (such as going to sleep and not waking up), doesn't sleep as well as usual, has been pacing more than an hour per day, can't sit still, feels extremely guilty most of the time, is unable to make some decisions, has lost more than 25 lb, and is exhausted almost all of the time. This has been going on for the past 13 weeks. The patient denies feeling sad and continues all his previous hobbies.

Clinical Pattern
Melancholic depression
Clinical Scenario
A 49-year-old man tells you "I am less interested in several of my usual activities and am so unhappy that I can't stand it. I feel I am inferior to most people. I frequently think of dying in passive ways (such as going to sleep and not waking up). I feel extremely slowed down physically, like I am stuck in mud. I frequently sleep at least 2 hours less than usual, waking up early in the morning before I would normally awaken. I get tired from doing almost anything. I've lost more than 25 lb. I get almost no pleasure from most of the activities that I usually enjoy, although when something pleasant happens or someone tries to cheer me up, I feel a little better but still feel somewhat depressed. My depression is regularly worse in the morning. I feel extremely guilty most of the time. There is a definite difference between this depression and the depression I would feel after someone close had died." This has been present for the past 8 weeks. His wife gave birth to a daughter 3 weeks ago.

Figure 2.—These clinical patterns and associated scenarios were created for this study.

TABLE 1.— *Residents (n= 35) Listing Criteria Symptoms and Episode Subtypes on Open-ended Questions*

Criteria Symptom	*Residents Listing Symptom, No. (%)*
Weight	34 (97)
Sleep disturbance	32 (91)
Loss of interest (mandatory)	30 (86)
Sad mood (mandatory)	28 (80)
Thoughts of death	21 (60)
Worthlessness/guilt	14 (40)
Impaired concentration	11 (31)
Fatigue	9 (26)
Psychomotor	7 (20)
Episode Subtype	Residents Listing Subtype
Melancholic	3 (9)
Catatonic	2 (6)
Postpartum	2 (6)
Seasonal	2 (6)
Atypical	1 (3)
Psychotic	13 (37)

in a separate booklet. The open-ended questions were as follows: "What are the symptoms of a major depressive episode enumerated in *DSM-IV*?" and "What are the subtypes of a major depressive episode in *DSM-IV*?"

The 21 clinical scenarios included 12 scenarios followed by the question, "Does this patient meet *DSM-IV* criteria for a major depressive disorder? (yes or no)." Four scenarios (1 for each level of severity) posed the question: "How severe is the patient's depression? (Choose the single best answer: mild, moderate, severe without psychosis, or severe with psychosis.)" Five scenarios (1 for each subtype) were used to evaluate the question, "Can you further subtype the patient's depression? (Choose the single best answer: atypical, catatonic, melancholic, postpartum, or seasonal.)" The scenarios appeared in random order in the booklet, with all diagnostic scenarios appearing before the classification scenarios.

Measurements

To assess knowledge of the diagnostic criteria for depression, we measured the percentage of subjects listing each of the diagnostic criteria symptoms. A symptom was considered correct if it is one of the criteria or if the *DSM-IV* mentions it as indicative of a criterion. To assess the knowledge of episode subtypes, we measured the percentage of subjects listing each of the subtypes. For the diagnoses of MDD and the classification of episode severity, we measured mean sensitivity and specificity per resident. For the classification of episode subtype, we determined only sensitivity. Specificity was not determined for episode subtype because the specificity depends on the definition of a noncase, for which there are several possibilities: patients with other diagnosable subtypes (a subset of patients), patients with MDE, or patients with MDD.

Results

Knowledge of Criteria Symptoms and Subtypes

Table 1 shows the percentage of residents listing each criterion symptom on the open-ended question. Weight change and sleep disturbance were the two most frequently listed symptoms. Slightly fewer residents listed the two mandatory symptoms, sad mood and loss of interest. Less than two thirds listed thoughts of death and feelings of decreased self-worth. The other symptoms, impaired concentration, fatigue, and psychomotor effects, were only listed by less than a third of the residents. Of the two mandatory symptoms, every resident listed at least one of them, and 23 residents listed them both. The distribution of the number of criteria symptoms listed by the residents is shown in Figure 3.

Few of the residents could list the episode subtypes on the open-ended question (Table 1). The most common answer, psychotic depression, is considered a level of severity and not a subtype in the *DSM-IV* classification.

Diagnosis of MDD and Classification of Episode Severity and Subtype

The mean sensitivity per resident for diagnosing MDD was 64% (SD = 33%; 95% confidence interval, 53%–75%), based on three scenarios per subject. The mean specificity was 69% (SD = 21%; 95% confidence interval, 62%–76%), based on nine scenarios per subject.

The distribution of responses, sensitivities, and specificities for classifying the levels of severity is shown in Table 2. The sensitivities for classification of moderate, severe, and psychotic episodes were lower than for mild episodes. For all levels of severity, specificity was higher than sensitivity. The presence of psychosis (that is, hallucinations or delusions) was most commonly noted with hallucinations and more often missed with delusions (data not shown). Of the 39 misclassified episodes, 30 were classified as less severe and 9 as more severe.

The sensitivity for the classification of subtype, based on one scenario of each subtype per resident, was 34% for atypical, 51% for catatonic, 74% for melancholic, 100% for postpartum, and 94% for seasonal.

Discussion

The goals of this study were to evaluate medical residents' knowledge of the symptoms and subtypes of major depression and to assess proficiency in diagnosing and classifying depressive episodes. We found that most resident physicians knew only a few of the diagnostic symptom criteria defined in *DSM-IV* and that sensitivity and specificity for the diagnosis were low. Sensitivity for the classification of episode severity was high for mild episodes and somewhat lower for moderate and severe episodes. The specificity for the classification of severity at all levels was fairly high. Most residents did not know the *DSM-IV* subtypes of MDE and, on scenarios, had difficulty determining episode subtype.

Residents' lack of knowledge of the criteria symptoms for MDD may be responsible for the low diagnostic

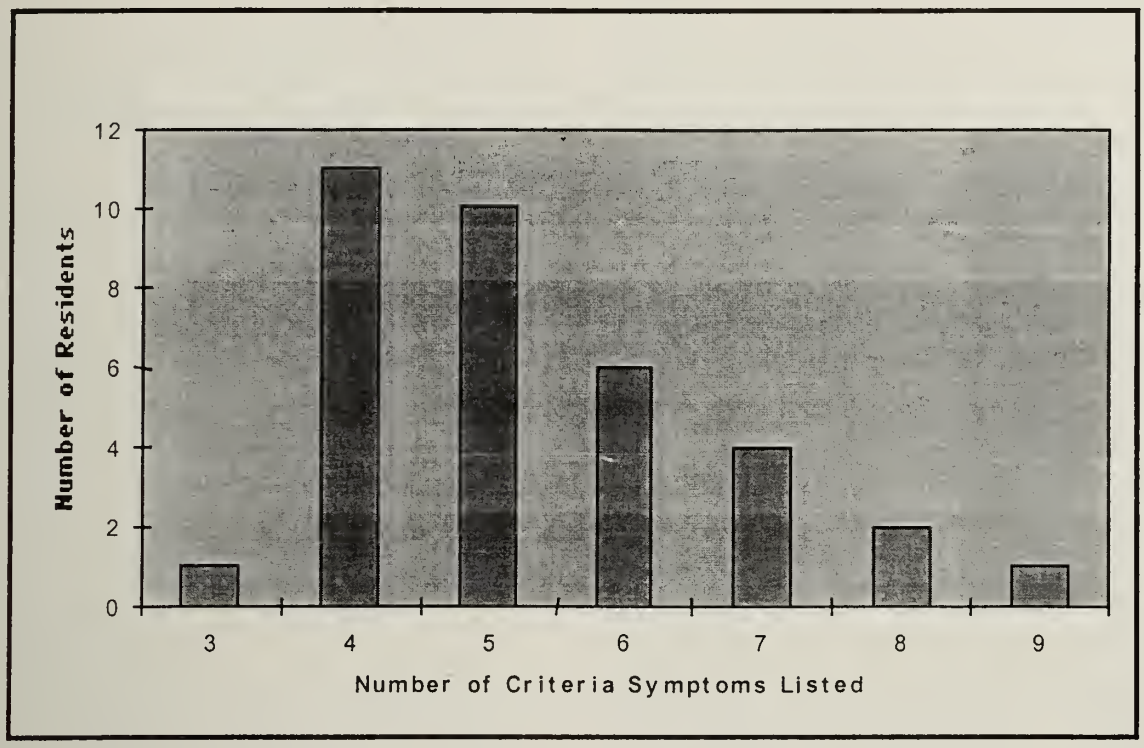


Figure 3.—Distribution of the number of criteria symptoms listed by residents.

accuracy we observed in this study and may also underlie to some extent the underrecognition of depression in primary care settings. The two mandatory symptoms, sad mood and loss of interest, were known by 28 (80%) and 30 (86%) residents, respectively. Twelve (34%) residents listed four or fewer of the criteria symptoms; five of the criteria are needed to make the diagnosis.

Two other studies have attempted to ascertain knowledge of the criteria symptoms for MDE. Rapp and Davis[26] also found poor recall of the diagnostic criteria in a survey of medical residents (with more stringent scoring criteria), ranging from 84% for "appetite/weight change" to 6% for "self-reproach, guilt," "diminished concentration," and "thoughts of death/suicide." Similarly, in a survey of 36 general practitioners, Bowers and co-workers[27] found low recall of the diagnostic symptoms, ranging from 28 (78%) for "insomnia or hypersomnia" to 2 (6%) for "feelings of worthlessness or guilt" and "recurrent thoughts of death or suicidal ideation." Failure to assess the appropriate symptoms of depression could lead to low diagnostic sensitivity or to low specificity.

Both the sensitivity and specificity for the diagnosis of depression were slightly less than 70%. Compared with previous studies evaluating the diagnosis of depression by residents in clinical settings,[1,2,4,5,10–12] we found a higher sensitivity and a lower specificity. These studies found sensitivities from 20.5% to 67% and specificities from 81% to 91%. The higher sensitivity and lower specificity we found may have been because our subjects could not be blinded to this study's focus on depression

TABLE 2.—*Distribution of Responses, Sensitivities, and Specificities for Classifying Severity of Depression Episodes**

	Residents' Classification (n = 35)					
Depressian	*Mild*	*Moderate*	*Severe*	*Psychatic*	*Mean Sensitivity (95% CI), %*	*Mean Specificity (95% CI), %*
DSM-IV Classification†						
Mild	30	5	0	0	86 (74–97)	92 (88–97)
Moderate	8	23	4	0	66 (50–82)	81 (74–88)
Severe	0	10	25	0	71 (56–87)	90 (84–95)
Psychotic	0	5	7	23	66 (50–82)	100

*CI = confidence interval, *DSM-IV = Diognostic and Statisticol Monuol of Mental Disorders, Fourth Edition*
†From the American Psychiatric Association.[22]

and thus were likely "primed" to diagnose depression. Moreover, evaluating hypothetical scenarios that present all relevant symptoms would also likely result in a higher sensitivity for diagnosing depression compared with assessing symptoms in actual patients.

Although several studies have evaluated whether physicians diagnose depression when it is present, none have determined whether physicians appreciate the severity or subtype of episodes of this disorder according to *DSM-IV*. Recognizing episode severity, however, is critical to optimal management, which primary care physicians are now expected to provide in many health care settings. The residents whom we evaluated were less likely to correctly perceive the severity of more serious (moderate, severe, or psychotic) episodes compared with milder episodes. The implications of failing to recognize moderate, severe, or psychotic episodes of depression as such are clear and potentially serious: these patients may be prone to undertreatment; may not receive needed antipsychotic medications; or may not have appropriate referrals to psychiatrists, especially in settings that discourage such referrals. Although classification errors were to adjoining levels of severity (for example, severe classified as moderate or mild classified as moderate), according to AHCPR guidelines, 64% (25 of 39) of these misclassifications would potentially result in undertreatment or overtreatment.

The ability of the subjects to spontaneously name the episode subtypes was extremely limited, and sensitivity for classifying atypical, catatonic, and melancholic episodes was low. Although subtype classification is emphasized by AHCPR guidelines, exact classification may be clinically less important than the correct recognition of episode severity. Yet, there are specific treatment recommendations for the different subtypes: atypical episodes respond better to monoamine oxidase inhibitors than to tricyclic antidepressants; catatonic episodes may require electroconvulsive therapy; melancholic episodes require either pharmacologic or electroconvulsive treatment and should not be treated only with psychotherapy; women with postpartum depression should be admitted to the hospital and treated medically; and seasonal depression may not respond to medication or psychotherapy, but phototherapy is an option for some patients.

The limitations of this study are principally related to the use of hypothetical cases. As noted earlier, this format may overestimate residents' ability to evaluate symptoms of depression (that is, symptom pursuit). In addition, because all participants were from a single training program, we cannot be sure that our results generalize to residents in other training programs.

This study is consistent with the large body of evidence indicating that non–mental health specialists frequently fail to recognize the presence or absence of major depression. We have further demonstrated that when evaluating hypothetical cases, medical residents often fail to appreciate the severity and type of depression presented, possibly leading to less-than-optimal treatment. Efforts to improve care for depression in primary care settings must, therefore, not focus solely on the recognition of depression but go further to allow greater diagnostic acuity. Just as primary care physicians must appreciate the differences between right- and left-sided heart failure and the severity of heart failure, so, too, must primary care physicians understand the more subtle aspects of major depression in their patients. Future educational and research initiatives should focus on developing methods that will not only increase primary care physicians' recognition of depression, but also enhance their appreciation of clinically important features of depression, such as episode severity and subtype.

REFERENCES

1. Moore JT, Silimperi DR, Bobula JA. Recognition of depression by family medicine residents: the impact of screening. J Fam Pract 1978; 7:509–513

2. Reifler BV, Okimoto JT, Heidrich FE, Inui TS. Recognition of depression in a university-based family medicine residency program. J Fam Pract 1979; 9:623–628

3. Nielsen AC III, Williams TA. Depression in ambulatory medical patients: prevalence by self-report questionnaire and recognition by nonpsychiatric physicians. Arch Gen Psychiatry 1980; 37:999–1004

4. Seller RH, Blascovich J, Lenkei E. Influence of stereotypes in the diagnosis of depression by family practice residents. J Fam Pract 1981; 12:849–854

5. Walker FB IV, Novack DH, Brynes G, Kaiser DL. Recognition of anxiety and depression by residents in a general medicine clinic. J Med Educ 1982; 57:195–197

6. Zung WWK, Michael MD, Moore JT, George DT. Recognition and treatment of depression in a family medicine practice. J Clin Psychiatry 1983; 44:3–6

7. Freeling P, Rao BM, Paykel ES, Sireling LI, Burton RH. Unrecognised depression in general practice. BMJ 1985; 290:1880–1883

8. German PS, Shapiro S, Skinner EA, et al. Detection and management of mental health problems of older patients by primary care providers. JAMA 1987; 257:489–493

9. Prestidge BR, Lake CR. Prevalence and recognition of depression among primary care outpatients. J Fam Pract 1987; 25:67–72

10. Block M, Schulberg HC, Coulehan JC, McClelland M, Gooding W. Diagnosing depression among new patients in ambulatory training settings. J Am Board Fam Pract 1988; 1:91–97

11. Henley CE, Coussens WR. The ability of family practice residents to diagnose depression in outpatients. J Am Osteopath Assoc 1988; 88:118–122

12. Sliman RJ, Donohue TA, Jarjoura D, Ognibene AJ. Recognition of depression by internal medicine residents. J Community Health 1992; 17:143–152

13. Weissman MM, Myers JK, Thompson D. Depression and its treatment in a US urban community. Arch Gen Psychiatry 1981; 38:417–421

14. Keller MB, Klerman GL, Lavori PW, Fawcett JA, Coryell W, Endicott J. Treatment received by depressed patients. JAMA 1982; 248:1848–1855

15. Keller MB, Lavori PW, Klerman GL, Andreasen NC, Endicott J, Coryell W, et al. Low levels and lack of predictors of somatotherapy and psychotherapy received by depressed patients. Arch Gen Psychiatry 1986; 43:458–466

16. Magruder-Habib K, Zung WWK, Feussner JR, Alling WC, Saunders WB, Stevens HA. Management of general medical patients with symptoms of depression. Gen Hosp Psychiatry 1989; 11:201–206

17. Katon W, Von Korff M, Lin E, Bush T, Ormel J. Adequacy and duration of antidepressant treatment in primary care. Med Care 1992; 30:67–76

18. Katon W, Von Korff M, Lin E, et al. Collaborative management to achieve treatment guidelines: impact on depression in primary care. N Engl J Med 1995; 273:1026–1031

19. Lin EHB, Von Korff M, Katon W, et al. The role of the primary care physician in patients' adherence to antidepressant therapy. Med Care 1995; 33:67–74

20. Depression in Primary Care. Vol 1: Detection and Diagnosis. Rockville (Md): US Dept of Health and Human Services, Public Health Service, Agency for Health Care Policy and Research; 1993. AHCPR publication No. 93-0550

21. Depression in Primary Care. Vol 2: Treatment of Major Depression. Rockville (Md): US Dept of Health and Human Services, Public Health Service, Agency for Health Care Policy and Research; 1993. AHCPR publication No. 93-0550

22. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Washington (DC): American Psychiatric Association; 1994

23. Zimmerman M, Coryell W, Corenthal C, Wilson S. A self-report scale to diagnose major depressive disorder. Arch Gen Psychiatry 1986; 43:1076–1081

24. Cohen J. A coefficient of agreement for nominal scales. Educ Psychol Meas 1960; 20:37–46

25. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977; 33:159–174

26. Rapp SR, Davis KM. Geriatric depression: physicians' knowledge, perceptions, and diagnostic practices. Gerontologist 1989; 29:252–257

27. Bowers J, Jorm AF, Henderson S, Harris P. General practitioners' reported knowledge about depression and dementia in elderly patients. Aust N Z J Psychiatry 1992; 26:168–174

Nonsurgical Causes of Pneumoperitoneum

RICHARD A. MULARSKI, MD; MICHAEL L. CICCOLO, MD; *and* WILLIAM D. RAPPAPORT, MD; *Tucson, Arizona*

The radiographic manifestation of free air in the peritoneal cavity suggests serious intra-abdominal disease and the need for urgent surgical management. Yet, about 10% of all cases of pneumoperitoneum are caused by physiologic processes that do not require surgical management. We retrospectively reviewed cases of nonsurgical causes of pneumoperitoneum at the 2 teaching hospitals of a university medical center between January 1990 and December 1995. Successful management by observation and supportive care without surgical intervention was defined as the diagnostic feature of nonperforation. Failure of a laparotomy to delineate a surgical cause or to result in a reparative procedure is congruent with a nonsurgical cause of pneumoperitoneum. During this period, 8 patients (6 men and 2 women; mean age, 61 years) were identified with nonsurgical causes of pneumoperitoneum. Two patients underwent negative laparotomy, and the other 6 were successfully managed nonoperatively and discharged from the hospital. In 6 patients, a cause of the pneumoperitoneum was identified. The causes may be grouped under the following categories: postoperatively retained air, thoracic, abdominal, gynecologic, and idiopathic. In our review of the literature, 61 of 139 reported cases underwent surgical treatment without evidence of perforated viscus. To avoid unnecessary surgical procedures, both primary medicine physicians and surgeons need to recognize nonsurgical causes of pneumoperitoneum. Conservative management is warranted in the absence of symptoms and signs of peritonitis.

(Mularski RA, Ciccolo ML, Rappaport WD. Nonsurgical causes of pneumoperitoneum. West J Med 1999; 170:41–46)

Pneumoperitoneum is a radiologic term denoting an abnormal collection of air in the peritoneal cavity. Radiographic evidence of free intraperitoneal air was linked to intra-abdominal disease in the early 1900s and continues to be a useful diagnostic tool for perforation of an intra-abdominal viscus.[1] About 85% of patients with a ruptured viscus will present with pneumoperitoneum, most often from a perforated gastric or duodenal ulcer, although perforated colon or small bowel may also present with pneumoperitoneum.[2–4] When a new onset of pneumoperitoneum is present in a patient with fever, abdominal pain, leukocytosis, and signs of peritonitis, surgical management is indicated.

Pneumoperitoneum without evidence of visceral perforation has been reported in 5% to 14% of all occurrences.[2,5,6] Often patients with this disorder undergo laparotomy without intraoperative evidence of visceral disease. Therefore, in atypical presentations or in patients with relevant historical evidence, nonsurgical causes of pneumoperitoneum should be considered. We reviewed cases of nonsurgical causes of pneumoperitoneum in inpatients at two major teaching hospitals of a university medical center from January 1990 to December 1995 and describe our clinical research to facilitate the examination of its clinical presentation, management, and outcome.

Report of Cases

Patient 1

The patient, a 65-year-old man, was admitted to the intensive care unit with pulmonary edema and respiratory failure requiring intubation. By hospital day 2, his chest radiograph and clinical course were consistent with the adult respiratory distress syndrome. High pressures were required to adequately ventilate the patient. Ventilatory management became normal by hospital day 26, and tracheostomy and gastrostomy were performed. On hospital day 39, pneumoperitoneum was noted on a chest radiograph. On physical examination, the patient's abdomen was slightly distended and nontender without peritoneal signs. Although not sufficient to exclude perforation, a radiographic examination with diatrizoate meglumine instilled through the gastrostomy tube failed to demonstrate extravasation. The patient was observed, and the amount of free air increased as bowel sounds were noted to decrease over the next 24 hours. A xenon lung perfusion scan demonstrated radioactive tracer beneath the right hemidiaphragm with the application of positive-pressure ventilation. The patient was conservatively managed and extubated one month later. The pneumoperitoneum increased over the course of a week

From the Oregon Health Sciences University (Dr Mularski) and the Department of Surgery, University of Arizona Health Sciences Center (Drs Ciccolo and Rappaport), Tucson, Arizona.

Reprint requests to William D. Rappaport, MD, Department of Surgery, University of Arizona Health Sciences Center, 1501 N Campbell Ave, Tucson, AZ 85724.

Figure 1.—Chest radiograph demonstrates free intraperitoneal air (Patient 4).

and then spontaneously resolved without the need to modulate ventilatory management or enteral feedings.

Patient 2

The patient, a 54-year-old man with a history of bipolar disorder and bullous emphysema, presented to the emergency department with intermittent, crampy, left upper abdominal quadrant pain. He did not have fever, chills, nausea, or vomiting and was afebrile with stable vital signs. No abdominal tenderness was present on physical examination. The leukocyte count was 12.5 × 10^9/liter, with an increase in the number of immature cells. Radiographs of the abdomen and chest revealed pneumoperitoneum. Computed tomography of the abdomen confirmed the presence of pneumoperitoneum and revealed an incidental renal mass but no cause for the free air. He was admitted to the hospital for observation. The following day, the leukocyte count returned to normal, the patient was advanced to a regular diet, and he was discharged on day 4 of his hospital stay. He reported a similar event 20 years ago that led to an exploratory laparotomy that elicited no abnormalities.

Patient 3

The patient, a 74-year-old man with a history of adrenal insufficiency who was admitted to the hospital for hypoxic encephalopathy, was noted to have free air under the right diaphragm following a cardiac arrest complicated by esophageal intubation. He was afebrile. On examination, he had a grossly distended abdomen with decreased bowel sounds and a suggestion of tenderness obscured by the encephalopathy. His leukocyte count was 10.9 ≤ 10^9/liter. An exploratory laparotomy was performed that demonstrated no evidence of perforation. The patient succumbed to progressive respiratory failure and died one month after admission.

Figure 2.—Computed tomography of the abdomen confirms pneumoperitoneum and demonstrates pneumatosis cystoides intestinalis and air in the portal vein (Patient 4).

Patient 4

The patient, a 70-year-old man with a history of ichthyosis vulgaris, presented with diffuse abdominal pain for the previous few weeks, increasing acutely, and occurring with anorexia the day before consultation. His medical history was relevant for radical prostatectomy and 35 Gy of radiation therapy for stage C adenocarcinoma of the prostrate eight months previously. Computed tomography of the abdomen six months before this presentation demonstrated no metastatic disease, although sigmoid diverticula were noted. He was afebrile, and an abdominal examination revealed no tenderness or peritoneal signs. His leukocyte count was within normal limits, but his chest and abdominal radiographs revealed free air under the diaphragm (Figure 1). Although not sufficient to exclude perforation, a limited upper gastrointestinal study with diatrizoate revealed no extravasation. Computed tomography of the abdomen revealed air in the wall of the left colon and free air in the porta hepatis and portal vein (Figure 2). The patient was conservatively managed and advanced slowly to a regular diet. He was discharged on day 4 of his hospital stay.

Patient 5

The patient, a 72-year-old woman with a history of scleroderma and secondary feeding difficulties, presented with abdominal pain, bloating, decreased appetite, and four days of constipation. She had coffee-ground emesis the morning of admission. She was afebrile with stable vital signs. On physical examination, she had decreased bowel sounds with tympany and tenderness in the left lower quadrant without peritoneal signs. A large amount of free air was present on a radiograph of the abdomen. Guaiac examination of a stool specimen and nasogastric lavage was negative for frank or occult bleeding, and the leukocyte count was 6.6 × 10^9/liter. The patient was managed medically with a regimen of omeprazole and remained clinically stable for the following two days, with resolving pneumoperitoneum. She was fed, and abdominal pain with bloating developed. Ultrasonography and computed tomography

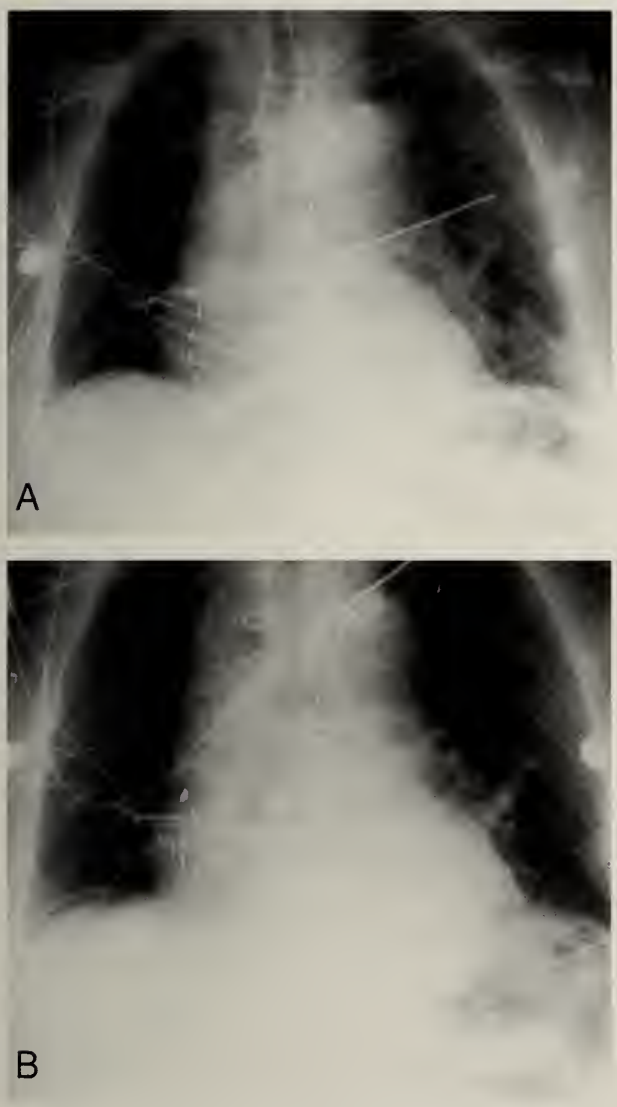


Figure 3.—Serial chest radiographs before (A) and after (B) nasogastric air insufflation of 600 ml, without a demonstrable increase in pneumoperitoneum (Patient 7).

of the abdomen and pelvis revealed multiple loops of fluid-filled bowel. A left pneumothorax subsequently developed, although a thoracostomy tube was not required. The pain and bloating resolved with the restriction of enteral feeding, and she was discharged on day 10 of her hospital stay on a regimen of parenteral nutrition and supplemental oxygen.

Patient 6

The patient, a 62-year-old man, presented one day following endoscopic polypectomy with increasing abdominal pain and pneumoperitoneum on abdominal radiograph. His temperature was 38.2°C, and he had otherwise normal vital signs. Physical examination of the abdomen revealed diffuse tenderness with localization of pain to the left side. The leukocyte count was 11.1 × 10^9/liter. He was admitted to the hospital, and a regimen of broad-spectrum intravenous antibiotics and intravenous hydration was started. He improved clinically over the next few days and was discharged on oral antibiotic therapy on day 5 of the hospital stay.

Patient 7

A 75-year-old man with a history of peptic ulcer disease was noted on postoperative day 2 of a coronary artery bypass graft to have pneumoperitoneum on routine chest roentgenogram. The patient was afebrile and reported mild abdominal tenderness. Bowel sounds were decreased, and mild to moderate epigastric tenderness was noted on examination. The leukocyte count was 23.8 × 10^9/liter. Air was instilled through a nasogastric tube without increase in the amount of free air noted on radiographs (Figure 3). Esophagogastroduodenoscopy revealed multiple erosive ulcers in his stomach, a hiatal hernia, and Barrett's esophagitis. He was conservatively managed and discharged after advancing to a regular diet.

Patient 8

The patient, a 17-year-old woman with a history of Raynaud's phenomenon, presented with midsternal chest pain radiating to the back of five days' duration and severe epigastric pain the day before admission. She was afebrile with stable vital signs, and abdominal examination revealed normal bowel sounds with slight distension, diffuse tenderness, and involuntary guarding. A chest roentgenogram revealed free intraperitoneal air with massive gastric distension and small bowel dilation. The leukocyte count was normal. An exploratory laparotomy was performed that showed no evidence of visceral perforation. She improved clinically and was discharged on day 5 of the hospital stay.

Discussion

Pneumoperitoneum usually denotes a perforation of an intra-abdominal viscus, but in about 10% of patients, a nonsurgical source is responsible for free air in the peritoneum and the radiographic findings. Surgical intervention is often performed in these patients that fails to demonstrate disease or result in a reparative procedure. In our review of the literature, 61 (44%) of 139 patients with reported nonsurgical pneumoperitoneum went to surgery without evidence of a perforated viscus.

In this retrospective series, eight patients with nonsurgical pneumoperitoneum were identified. Two patients underwent laparotomy that elicited no abnormalities, and the remaining six were successfully managed nonoperatively and discharged from the hospital (Table 1). The major etiologic mechanisms may be grouped under the following categories: postoperatively retained air, thoracic, abdominal, gynecologic, and idiopathic (Table 2).

Free intra-abdominal air following an abdominal surgical procedure is a common and expected occurrence. Pneumoperitoneum may be recognized on roentgenography for as long as four weeks following an intra-abdominal procedure, although complete resorption

TABLE 1.—*Patient Characteristics and Cause of Pneumoperitoneum**

Patient	Age, y	Sex	Assaciatian(s)	Cause	Categary
1	65	M	ARDS, high airway pressures	IPPV	Thoracic
2	54	M	Bullous emphysema	Rupture of blebs	Thoracic
3	74	M	CPR, esophageal intubation	CPR	Thoracic
4	70	M	Diverticulosis, irradiation to pelvis	PCI	Abdominal
5	72	F	Scleroderma	PCI versus CVD	Abdominal
6	62	M	Colonoscopy and polypectomy	Postpolypectomy syndrome	Abdominal
7	75	M	Peptic ulcer disease, CABG	?Subclinical perforation	Idiopathic
8	17	F	Raynaud's phenomenon, bowel dilation	?Subclinical perforation	Idiopathic

*ARDS = adult respiratory distress syndrome, CABG = coronary artery bypass grafting, CPR = cardiopulmonary resuscitation, CVD = collagen vascular disease, IPPV = intermittent positive-pressure ventilation, PCI = pneumatosis cystoides intestinalis

usually occurs within the first week.[7] Following laparoscopic procedures, nearly 50% of patients will have air within the peritoneal cavity detected radiographically.[8]

TABLE 2.—*Causes of Pneumoperitoneum*

Categary	Mechanism
Postoperative	Retained air from open laparotomy
	Retained air from laparoscopy
Thoracic	Intermittent positive-pressure ventilation
	Barotrauma
	Increased intrathoracic pressure—cough, retching Valsalva maneuver
	Asthma
	Bronchoscopy
	Cardiopulmonary resuscitation and mouth-to-mouth ventilation
	Adenotonsillectomy
	Pulmonary tuberculosis
	Blunt trauma
	Bronchopulmonary fistula
	Spontaneous rupture of pulmonary blebs
Abdominal	Pneumatosis cystoides intestinalis
	Endoscopic procedures
	Postpolypectomy syndrome
	Peritoneal dialysis
	Collagen vascular disease
	Pneumocholecystitis
	Jejunal and sigmoid diverticulosis
	Distended hollow viscus
	Subclinical perforated viscus
Gynecologic	Vaginal insufflation
	Knee-chest exercises
	Pelvic inflammatory disease
	Coitus
	Gynecologic examination procedures
	Vaginal douching
Idiopathic	

Decreasing amounts of air are expected in either open or laparoscopic cases, and thus, a protracted and increasing pneumoperitoneum in the presence of abdominal pain may indicate a complication of a perforated viscus and the need for surgical exploration.

Spontaneous pneumoperitoneum from an intrathoracic route is the most frequently reported cause in nonsurgical peritoneal air collections.[3–5,9,10] Intermittent positive-pressure ventilation may lead to air being introduced into the abdominal cavity by direct passage through microscopic pleural and diaphragmatic defects or through the mediastinum along the perivascular connective tissue, traveling retroperitoneally, and then rupturing into the peritoneal cavity.[9,11,12] The risk of pneumoperitoneum during ventilatory support correlates with peak inspiratory pressures above 40 cm of water and positive end-expiratory pressures above 6 cm of water.[4] Other risk factors for barotrauma and subsequent pneumoperitoneum with positive-pressure ventilation include large tidal volumes, noncompliant lungs, and preexisting pulmonary disease, most notably obstructive airway disease and the adult respiratory distress syndrome.[9,13] In patients receiving ventilatory support who have a new onset of pneumoperitoneum, the presence of air itself may cause pain and peritoneal irritation, although generally of less severity than in visceral perforation.[14,15] The report of patient 1 illustrates the thoracic route for nonsurgical pneumoperitoneum and the use of a xenon lung scan for demonstrating extravasation of radioactive tracer beneath the diaphragm with positive-pressure ventilation. Other causes of pneumoperitoneum by the thoracic route include asthma,[16] spontaneous rupture of pulmonary blebs (Patient 2),[17] pulmonary tuberculosis,[18] and blunt trauma.

Iatrogenic causes of pneumoperitoneum that share the mechanism of increased tracheal pressure include insufflation during bronchoscopy and mouth-to-mouth resuscitation.[13,19–21] Cardiopulmonary resuscitation may result in abdominal free air due to the combination of increased airway pressure and the application of blunt force to the chest.[19–21] A rare phenomenon of tension pneumoperitoneum has been described as a complication of

positive-pressure ventilation and cardiopulmonary resuscitation that, without urgent decompression, rapidly progresses to hemodynamic collapse.[22,23] As in Patient 3, a lowered threshold for surgery based on the inability to perform a reliable physical examination may lead to a high "negative laparotomy" rate in these patients.

The most common abdominal cause of nonsurgical pneumoperitoneum is pneumatosis cystoides intestinalis, also referred to as cystic lymphomatosis or enteromesenteric emphysema.[9,24–26] Pneumatosis cystoides intestinalis is characterized by multiple intramural gas-filled cysts that may be throughout the gastrointestinal tract but are most commonly found at the terminal ileum.[27,28] The condition is generally benign and asymptomatic, although nonspecific complaints such as vomiting, diffuse abdominal pain, diarrhea, abdominal distension, and tenesmus are seen in less than 15% of patients.[27,28] Pneumatosis cystoides intestinalis is generally found in conjunction with other primary disease processes, including chronic obstructive pulmonary disease and inflammatory bowel disease. As Macklin demonstrated, any thoracic disease that might introduce air into the mediastinal route could lead to pneumatosis cystoides intestinalis.[11] When the cysts rupture, a pneumoperitoneum may be produced with a spectrum of symptoms ranging from asymptomatic to acute abdominal pain. The condition generally resolves spontaneously but may be indolent and recurrent. Treatment with hyperbaric oxygen and antibiotics has demonstrated some efficacy in reducing long-term symptoms from this disease. In the short term, as in Patient 4, conservative and watchful management is generally sufficient.[25]

Cases of atypical pneumatosis cystoides intestinalis or an as-yet-undefined process of the gastrointestinal tract are reported in collagen vascular diseases such as scleroderma, systemic lupus erythematosus, and mixed connective tissue disorder.[25,26,29] As in Patient 5 of our series, it is difficult to clearly establish the presence of pneumatosis cystoides intestinalis in all patients, but with a relevant etiologic condition, attempted conservative management is appropriate in the absence of peritonitis. However, cases of pneumatosis cystoides intestinalis in immunosuppressed patients that evolved rapidly into enteric infection, bowel ischemia, and death have been reported.[25,30] Caution is also warranted in infants, in whom pneumatosis cystoides intestinalis is mimicked by necrotizing enterocolitis.[24]

Air insufflation, forceful manipulation, and excessive electrocautery in endoscopy have also been linked to the development of pneumoperitoneum.[31,32] Microperforations may allow air to escape under high pressures without extravasation of intestinal contents. Pneumoperitoneum may be detectable in as many as 0.1% of endoscopic procedures, and although pneumoperitoneum was initially thought to be an indication for laparotomy, conservative management is generally warranted in the absence of peritoneal signs.[32,33]

Rare causes following the abdominal route include pneumocholecystitis,[34] jejunal and sigmoid diverticulosis,[35,36] and fecal impaction or distended hollow viscus.[16,37] It is proposed that air can leak under pressure from thinned, intact bowel wall without demonstrable or clinically substantial perforation.

A phenomenon labeled postpolypectomy syndrome has been described in transmural burns of the colon following polypectomy and may rarely be associated with pneumoperitoneum.[38,39] Patients with the syndrome generally present with fever, abdominal pain, and localized peritoneal signs following endoscopy. Conservative management by hospital admission, the cessation of oral intake, intravenous antibiotic therapy, and hydration has been reported. Patient 6 had a typical presentation of postpolypectomy syndrome, and this case provides an example of successful management by observation and appropriate antibiotic therapy. Failure to improve or worsening of symptoms require a laparotomy.

It has been proposed in idiopathic pneumoperitoneum, especially in the presence of a "negative laparotomy," that a subclinical microperforated hollow viscus may have been present.[5,35,40] For a nonsurgical pneumoperitoneum to develop by this mechanism and resolve with conservative management, the leak must be small enough to permit the escape of gas without the evolution of bowel contents, and it must occur in a patient whose resistance to infection is intact. As in Patients 7 and 8 of our series, pneumoperitoneum may have evolved from subclinical perforation or be due to other factors that remained enigmatic.

Gynecologic causes, although rare compared with the previously described causes, illustrate another mechanism whereby air can pass upward (through the fallopian tubes) into the peritoneum. Specific examples include vaginal insufflation by orogenital sex,[41] vaginal douching,[42] postpartum knee-chest exercises,[43] the use of bulb aspiration in pelvic examinations,[44] pelvic inflammatory disease,[45] and coitus.[46]

Conclusion

Most patients with nonsurgical pneumoperitoneum have historical clues or associated conditions that may indicate to the physician the possibility of this diagnosis. When abdominal pain and distension are minimal and peritoneal signs, fever, and leukocytosis are absent, nonsurgical causes of pneumoperitoneum should be considered.

Our recommendations are to remain alert for nonsurgical causes and, when such processes are considered, to attempt conservative management with supportive care and careful observation. Frequent reevaluation may preclude surgical intervention in all but the sickest patients to allow the clinical course to declare itself. Caution must be exercised in maintaining strict vigilance, especially in immunosuppressed patients, in whom signs of peritonitis may be occult and the course rapid and grave. By acquiring a working knowledge of the wide array of possible causes of pneumoperitoneum and their mechanisms, physicians can more successfully avoid resorting to unnecessary laparotomy and its associated morbidity.

REFERENCES

1. Dandy WE. Pneumoperitoneum. Ann Surg 1916; 70:378–383

2. McGlone FB, Vivion CG, Meir L. Spontaneous pneumoperitoneum. Gastroenterology 1966; 51:393–398

3. Kornblum SA. Radiographic pneumoperitoneum in acute perforation of the gastrointestinal tract. N Y J Med 1948; 48:2726–2728

4. Hillman KM. Pneumoperitoneum—a review. Crit Care Med 1982; 19:476–481

5. Roh JJ, Thompson JS, Harned RK, Hodgson PE. Value of pneumoperitoneum in the diagnosis of visceral perforation. Am J Surg 1983; 146:830–833

6. Winek TG, Mosely HS, Grout G, Luallin D. Pneumoperitoneum and its association with ruptured abdominal viscus. Arch Surg 1988; 123:709–712

7. Harrison I, Litwer H. Studies of the incidence and duration of postoperative pneumoperitoneum. Ann Surg 1957; 145:591–594

8. Millitz K, Moote DJ, Sparrow RK, Girotti MJ, Holliday RL, McLarty TD. Pneumoperitoneum after laparoscopic cholecystectomy: frequency and duration as seen on upright chest radiographs. AJR Am J Roentgenol 1994; 163:837–839

9. Gutkin Z, Iellin A, Meged S, Sorkine P, Geller E. Spontaneous pneumoperitoneum without peritonitis. Int Surg 1992; 77:219–223

10. Mezghebe HM, Leffall LD Jr, Siram SM, Syphax B. Asymptomatic pneumoperitoneum diagnostic and therapeutic dilemma. Am Surg 1994; 60:691–694

11. Macklin CC. Transport of air along sheaths of pulmonic blood vessels from alveoli to mediastinum. Arch Intern Med 1939; 64:913–926

12. Kleinman PK, Brill PW, Whalen JP. Anterior pathway for transdiaphragmatic extension of pneumomediastinum. AJR Am J Roentgenol 1978; 131:271–275

13. Glauser FL, Bartlett RH. Pneumoperitoneum in association with pneumothorax. Chest 1974; 66:536–540

14. Kreel L. Pneumoperitoneum. Postgrad Med 1986; 62:31–32

15. Steigman F, Singer HA. Spontaneous pneumothorax simulating acute abdominal affections. Am J Med Sci 1936; 192:67–72

16. van Gelder HM, Allen KB, Renz B, Sherman R. Spontaneous pneumoperitoneum: a surgical dilemma. Am Surg 1991; 57:151–156

17. Paira SO, Roverano S. Bilateral pneumothorax and mediastinal emphysema in systemic lupus erythematosus. Clin Rheumatol 1992; 11:571–573

18. Britt CI, Christoforidis AJ, Andrews NC. Asymptomatic spontaneous pneumoperitoneum. Am J Surg 1961; 101:232–235

19. Parke TRJ. Unexplained pneumoperitoneum in association with basic cardiopulmonary resuscitation efforts. Resuscitation 1993; 26:177–181

20. Krischer JP, Fine EG, Davis JH, Nagel EL. Complications of cardiac resuscitation. Chest 1987; 92:287–291

21. Atcheson SG, Petersen GV, Fred HL. Ill-effects of cardiac resuscitation: report of two unusual cases. Chest 1975; 67:615–616

22. Chitchley LAH, Rowbottom S. Fatal tension pneumoperitoneum with pneumothorax. Anaesth Intens Care 1994; 11:298–299

23. Higgins JRA, Haplin DMG, Midgley AK. Tension pneumoperitoneum: a surgical emergency. Br J Hosp Med 1988; 39:160–161

24. Chandler JG, Berk RN, Golden GT. Misleading pneumoperitoneum. Surg Gynecol Obstet 1977; 144:163–174

25. Daly BD, Guthrie JA, Couse NF. Pneumoperitoneum without peritonitis. Postgrad Med J 1991; 67:999–1003

26. Longo WE, Ballantyne GH, Graham AJ. Pneumatosis cystoides intestinalis: presentation as an acute abdomen. J Clin Gastroenterol 1987; 9:571–573

27. Keyting WS, McCarver RR, Kovarik JL, Daywitt AL. Pneumatosis intestinalis: a new concept. Radiology 1961; 76:733–741

28. Wolloch Y, Dintsman M, Weiss A, Tiqva P. Pneumatosis cystoides intestinalis of adulthood. Arch Surg 1972; 105:723–726

29. Pun YLW, Russell DM, Taggart GJ, Barraclough DRE. Pneumatosis intestinalis and pneumoperitoneum complicating mixed connective tissue disease. Br J Rheumatol 1991; 30:146–149

30. Day DL, Ramsay NK, Letourneau JG. Pneumatosis intestinalis after bone marrow transplantation. AJR Am J Roentgenol 1988; 151:85–87

31. Ylvisaker RS, Myhre J. Management of pneumoperitoneum after gastroscopy. Gastroenterology 1951; 18:463–465

32. Silvis SE, Nebel O, Rogers G, Sugawa C, Mandelstam P. Endoscopic complications: results of 1974 American Society for Gastrointestinal Endoscopy Survey. JAMA 1976; 235:928–930

33. Taylor R, Weakley FL, Sullivan BH Jr. Non-operative management of colonoscopic perforation with pneumoperitoneum. Gastrointest Endosc 1978; 24:124–125

34. Watson DI, Isaacs J, Williams RS. Emphysematous cholecystitis can cause pneumoperitoneum. Aust N Z J Surg 1994; 64:130–131

35. Simpson AJ. Spontaneous asymptomatic pneumoperitoneum secondary to jejunal diverticulosis. J Med Soc N J 1976; 73:1065–1067

36. Dunn V, Nelson J. Jejunal diverticulosis and chronic pneumoperitoneum. Gastrointest Radiol 1979; 4:165–168

37. Ferrara BE, Harrison WD. Pneumoperitoneum. J Fla Med Assoc 1991; 78:81–84

38. Ecker MD, Goldstein M, Hoexter B, Hyman RA, Naidich JB, Stein HL. Benign pneumoperitoneum after fiberoptic colonoscopy: a prospective study of 100 patients. Gastroenterology 1977; 73:226–230

39. Nitvatvongs S. Complication of colonoscopic polypectomy: an experience with 1555 polypectomies. Dis Colon Rectum 1986; 29:825–830

40. Hoover EL, Cole GD, Mitchell LS, Adams CZ Jr, Hassett J. Avoiding laparotomy in nonsurgical pneumoperitoneum. Am J Surg 1992; 164:99–103

41. Varon J, Laufer MD, Sternbach GL. Recurrent pneumoperitoneum following vaginal insufflation. Am J Emerg Med 1991; 9:447–448

42. Gantt CB Jr, Daniel WW, Hallenbeck GA. Nonsurgical pneumoperitoneum. Am J Surg 1977; 134:411–414

43. Lozman H, Newman AJ. Spontaneous pneumoperitoneum occurring during post partum exercises in the knee-chest position. Am J Obstet Gynecol 1956; 72:903–905

44. Cass LJ, Dow EC, Brooks JR. Pneumoperitoneum following pelvic examination. Am J Gastroenterol 1966; 45:209–211

45. Miller RE. The radiological evaluation of intraperitoneal gas (pneumoperitoneum). CRC Crit Rev Radiol Sci 1973; 4:61–85

46. Tabrisky J, Mallin LP, Smith JA III. Pneumoperitoneum after coitus: a complication due to uterine tube prolapse after vaginal hysterectomy. Obstet Gynecol 1972; 40:218–220

Alerts, Notices, and Case Reports

Cocaine-Induced Intestinal Ischemia

MUHAMMAD A. WATTOO, MD
OLUSOLA OSUNDEKO, MD
Philadelphia, Pennsylvania

COCAINE, AN ALKALOID derived from the *Erythroxylon coca* plant, remains a popular recreational drug.[1] Although its recreational use has decreased, the number of hard-core regular users remains unchanged at 476,000 according to the 1993 National Institute on Drug Abuse Household Survey.[2] Cocaine-related complications are, therefore, of clinical importance. Bowel ischemia due to cocaine use is probably more common than is reported, but it may be overlooked because its presentation is similar to other acute abdominal conditions. A direct causal relationship between cocaine use and bowel ischemia is difficult to prove. Nevertheless, the patients described in published reports so far had been relatively young, had a positive urine toxicology screen for cocaine, and had no previous history of atherosclerosis. We report a case of acute small bowel ischemia in the oldest patient after smoking crack cocaine.

Report of a Case

The patient, a 50-year-old man who smoked cigarettes and crack cocaine regularly, presented to the emergency department with a three-day history of abdominal pain, nausea, vomiting, and poor urine output after a binge of alcohol and cocaine use. The abdominal pain was sudden in onset, severe in intensity, and located mainly in the lower abdomen. The pain was made worse by oral intake and had no relieving factors. There was no history of fever, chills, chest pain, back pain, shortness of breath, or seizures. He had been unable to eat or drink for three days because of the pain.

On examination, the patient was awake and alert but looked uncomfortable. Apart from tachycardia (115 beats per minute), he had normal vital signs. He was clinically dehydrated. He had diffuse tenderness in the lower abdomen with guarding in his right lower quadrant, but no rebound was elicited at this stage. Bowel sounds were markedly diminished, and a rectal examination showed occult blood in the stool. Pertinent laboratory data included the following values: a leukocyte count of 30×10^9 per liter (30,000 per µl) with a leftward shift; hemoglobin level, 185 grams per liter (18.5 grams per dl); hematocrit, 0.55 (55%); platelet count, 300×10^9 per liter (300,000 per µl); serum bicarbonate, 19 mmol per liter; blood urea nitrogen, 16.4 mmol per liter (46 mg per dl); creatinine, 582 µmol per liter (6.6 mg per dl); phosphate, 3.13 mmol per liter (9.7 mg per dl; normal, 0.80–1.55 mmol per liter); and anion gap, 28. Other laboratory results were a creatine kinase level of greater than 16,000 units per liter (normal, 20–315); lactate dehydrogenase level, 9,282 units per liter (normal, 111–217); aspartate aminotransferase, 1,996 units per liter (normal, 3–26); alanine aminotransferase, 580 units per liter (normal, 5–30); alkaline phosphatase, 144 units per liter (normal, 25–128); amylase, 270 units per liter (normal, 30–120); and lipase, 144 units per liter (normal, 0–200). A urinalysis revealed 1-plus ketones, 3-plus blood and protein, 40 to 50 white blood cells per high-powered field, and few bacteria. The findings of urine microscopy were consistent with acute tubular necrosis.

Abdominal roentgenogram showed only a nonspecific bowel gas pattern. Computed tomography showed abdominal ascites and fluid collection or inflammatory changes (or both) in the right lower quadrant. The patient was admitted to the intensive care unit and was given fluid resuscitation and antibiotics. After a few hours, the patient became febrile, his abdominal pain worsened, and he had abdominal distension, generalized rebound tenderness, and absent bowel sounds. The patient underwent an exploratory laparotomy that revealed gangrenous distal small bowel, including the distal ileum. A 75-cm segment of the nonviable bowel was resected, and an end-to-end anastomosis was done. Microscopic examination of the specimen of resected bowel revealed acute ischemic necrosis of the small bowel wall. There was no thrombus, embolus, or atherosclerosis. The patient received hemodialysis, his renal function improved gradually, and he was subsequently discharged.

Discussion

We searched MEDLINE for the literature on cocaine-induced bowel ischemia.[3–17] The review excluded those who swallowed condom-filled cocaine packets with the intention of smuggling the drug—the so-called body packers. There were 18 cases to date, with most patients in their third or fourth decade of life. Our patient was the oldest at 50 years of age. There was nearly a 2:1 ratio of women to men. No method of administering cocaine is safe. Apart from two patients whose route of administration was unknown, most patients either smoked crack cocaine or injected it intravenously. Most cases involved ischemia of the small rather than the large bowel, and two thirds of the patients recovered, usually with surgical management (Table 1).

(Wattoo MA, Osundeko O. Cocaine-induced intestinal ischemia. West J Med 1999; 170:47–49)

From the Department of Internal Medicine, University of Pennsylvania Health System, Presbyterian Medical Center, Philadelphia, Pennsylvania.

Reprint requests to Olusola Osundeko, MD, Department of Internal Medicine, University of Pennsylvania Health System, Presbyterian Medical Center, 39th and Market Sts, Philadelphia, PA 19106 (e-mail: Olusola@yahoo.com).

TABLE 1.—*Reported Cases of Cocaine-Induced Bowel Ischemia**

Reference	Age, y	Sex	Route	Site of Ischemia	Outcome
This report	50	M	Smoked crack	Small bowel	Survived
Sudhakar et al, 1997[3]	35	F	Unknown	Small bowel	Died
Sudhakar et al, 1997[3]	32	F	IV	Small bowel	Survived
Boutros et al, 1997[4]	36	F	Smoked crack	Large bowel	Survived
Myers et al, 1996[5]	29	F	IV, smoked crack	Celiac artery thrombosis, mesenteric ischemia	Survived
Myers et al, 1996[5]	35	F	IV	Distal ileum, cecum	Survived
Jawahar et al, 1995[6]	31	F	Intranasal	Small bowel	Died
Yang et al, 1991[7]	26	F	Smoked crack	Large bowel	Survived
Freudenberger et al, 1990[8]	38	M	IV	Small bowel	Died
Mizrahi et al, 1988[9]	27	M	Intranasal	Small bowel	Survived
Endress et al, 1992[10]	30	F	Smoked crack	Small bowel	Survived
Hazanas et al, 1993[11]	23	F	Oral	Large bowel	Died
Hon et al, 1990[12]	37	F	Smoked crack	Small bowel	Survived
Garfia et al, 1990[13]	24	M	Not specified	Small bowel	Died
Martin, 1991[14]	30	M	Intranasal	Bowel	Survived
Brown et al, 1994[15]	47	M	IV	Large bowel	Survived
Fishel et al, 1985[16]	37	M	Smoked crack	Cecum and ascending colon	Survived
Nalbandian et al, 1985[17]	29	F	Oral	Small bowel	Survived
Nalbandian et al, 1985[17]	26	F	Oral	Distal small bowel and proximal colon	Died

*IV = intravenous injection

In keeping with previously described patients, our patient had no history of predisposing factors that make other causes of bowel ischemia likely. An additional factor may be cigarette smoking, a common finding among those who use cocaine. The combined use of cocaine and smoking has a probable additive effect on coronary artery vasoconstriction.[18] This may be applicable to other vessels elsewhere in the body, including mesenteric vessels. Our patient had been smoking for many years and was a current smoker at the time of his illness.

This patient had rhabdomyolysis that resolved with medical treatment. We had expected rhabdomyolysis to be a common complication among patients with bowel ischemia because ischemia is its most frequent cause.[19] Rhabdomyolysis, however, may be rare or underreported because there is only one reported case linking it to bowel ischemia.[8] We suggest that rhabdomyolysis should be screened for in all these patients because it may cause acute renal failure.[19]

Cocaine is a well-known central nervous stimulant, local anesthetic, and pyrogenic agent. Several mechanisms have been proposed to explain how cocaine causes bowel ischemia. It potentiates the normal adrenergic response by blocking the reuptake of presynaptic monoamine neurotransmitters.[20] Mesenteric vessels contain many α-adrenergic receptors.[21] Stimulation of these receptors causes intense vasoconstriction, leading to reduced blood flow and ischemia. Cocaine also has a direct vasoconstrictive effect by enhancing calcium flux across the endothelial membrane.[22] Some investigators have suggested that cocaine has a direct toxic effect on the gut mucosa.[23] Cocaine displaces the transmitter from the axonal membrane, thereby inducing a sympathomimetic response.[24] Thrombus formation and platelet aggregation are enhanced following cocaine administration.[25] Cocaine also decreases fibrinolytic activity by stimulating plasminogen activator inhibitor activity.[26] Some or all of these effects of cocaine may explain the increased susceptibility of the bowel to ischemia in patients who abuse this drug.

This report highlights the importance of including cocaine use in the differential diagnosis of acute abdomen in all patients. That our patient was 50 years old suggests that probably no age barriers to drug abuse exist. Many cases may go unrecognized for different reasons. Some patients may be reluctant to admit to cocaine use, drug testing is not uniform, and dose-related complications are not consistent.[27]

REFERENCES

1. Catterall W, Mackie K. Local anesthetics. In Hardman JG, Limbird LE, Molinoff PB, Ruddon RW, Gilman AG (Eds): The Pharmacological Basis of Therapeutics. 9th ed. New York, McGraw-Hill, 1996, pp 331–347

2. Substance Abuse and Mental Health Services Administration, Office of Applied Statistics. National Institute of Drug Abuse Household Survey, 1993. Rockville, Md, National Institute on Drug Abuse, US Dept of Health and Human Services, 1994

3. Sudhakar CB, Al-Hakeem M, MacArthur JD, Sumpio BE. Mesenteric ischemia secondary to cocaine abuse: case reports and literature review. Am J Gastroenterol 1997; 92:1053–1054

4. Boutros HH, Pautler S, Chakrabarti S. Cocaine-induced ischemic colitis with small-vessel thrombosis of colon and gallbladder. J Clin Gastroenterol 1997; 24:49–53

5. Myers SI, Clagett GP, Valentine RJ, Hansen ME, Aditi A, Arun C. Chronic intestinal ischemia caused by intravenous cocaine use: report of two cases and review of the literature. J Vasc Surg 1996; 23:724–729

6. Jawahar D, Leo PJ, Anandarao N, Pachter BR. Cocaine-associated intestinal gangrene in a pregnant woman. Am J Emerg Med 1997; 15:510–512

7. Yang RD, Han MW, McCarthy JH. Ischemic colitis in a crack abuser. Dig Dis Sci 1991; 36:238–240

8. Freudenberger RS, Capell MS, Hutt DA. Intestinal infarction after intravenous cocaine administration. Ann Intern Med 1990; 113:715–716

9. Mizrahi S, Laor D, Stamier B. Intestinal ischemia induced by cocaine abuse (Letter). Arch Surg 1988; 123:394

10. Endress C, Gary DGK, Wollschlaeger G. Bowel ischemia and perforation after cocaine use. AJR Am J Roentgenol 1992; 159:73–75

11. Hazanas FH, Torres CP, Delgado FI. Multiorgan failure and intestinal ischemia after cocaine intoxication (Letter). Intensive Care Med 1993; 19:239–240

12. Hon DC, Salloum LJ, Hardy HW III, Barone JE. Crack-induced enteric ischemia. N J Med 1990; 87:1001–1002

13. Garfia A, Valverde JL, Borondo JC, Candenas I, Lucena J. Vascular lesions in intestinal ischemia induced by cocaine-alcohol abuse: report of a fatal case due to overdose. J Forensic Sci 1990; 35:740–745

14. Martin TJ. Cocaine-induced mesenteric ischemia. N C Med J 1991; 52:429–430

15. Brown DN, Rosenholtz MJ, Marshall JB. Ischemia colitis related to cocaine abuse. Am J Gastroenterol 1994; 89:1558–1561

16. Fishel R, Hamamato G, Barbul A. Cocaine colitis: is this a new syndrome? Dis Colon Rectum 1985; 28:264–266

17. Nalbandian H, Sheth N, Dietrich R, Georgiou J. Intestinal ischemia caused by cocaine ingestion: report of two cases. Surgery 1985; 97:374–376

18. Moliterno DJ, Willard JE, Lange RA, Negus BH, Boehrer JD, Glamann DB, et al. Coronary-artery vasoconstriction induced by cocaine, cigarette smoking, or both. N Engl J Med 1994; 330:454–459

19. Veenstra J, Smit WM, Krediet RT, Arisz L. Relationship between elevated creatine phosphokinase and the clinical spectrum of rhabdomyolysis. Nephrol Dial Transplant 1994; 9:637–641

20. Isner JM, Chokshi SK. Cocaine and vasospasm. N Engl J Med 1989; 321:1604–1606

21. Collis MG. Vascular reactivity to adrenaline and angiotensin-II in the rat perfused mesenteric vasculature. Cardiovasc Res 1975; 9:118–126

22. Lange RA, Cigarroa RG, Yancy CW Jr, Willard JE, Popma JJ, Sills MN et al. Cocaine-induced coronary-artery vasoconstriction N Engl J Med 1989; 321:1557–1562

23. Hebra A, Brown MF, McGeehin K, O'Niell JA Jr, Ross AJ III. Systemic and mesenteric vascular effects of platelet-activating factor and cocaine: *in vivo* effects on a neonatal swine model. Am Surg 1993; 59:50–54

24. Gourgoutis G, Das G. Gastrointestinal manifestations of cocaine addiction. Int J Clin Pharmacol Ther 1993; 32:136–141

25. Rezkalla SH, Mazza JJ, Kloner RA, Tillema V, Chang S. The effect of cocaine on human platelets. Am J Cardiol 1993; 72:243–246

26. Moliterno DJ, Lange RA, Gerard RD, Willard JE, Lackner C, Hillis LD. Influence of intranasal cocaine on plasma constituents associated with endogenous thrombosis and thrombolysis. Am J Med 1994; 96:492–496

27. Jentzen J. Medical complications of cocaine abuse. Am J Clin Pathol 1993; 100:475–476

Potentiation of Warfarin Sodium by Amiodarone-Induced Thyrotoxicosis

KENNETH A. WOEBER, MD, FRCPE
IRVING WARNER, MD
San Francisco, California

THE ANTICOAGULANT EFFECT of warfarin sodium is influenced by several disease states, most notably renal and hepatic dysfunction, and by pharmacokinetic interactions with drugs that either induce or inhibit the hepatic microsomal mixed-function oxidase system.[1] Although thyrotoxicosis has been reported to potentiate the anticoagulant effect of warfarin, necessitating a reduction in dosage,[2–4] this phenomenon is not generally appreciated because the dosage requirements of most other drugs are increased in patients with thyrotoxicosis.[5] We report the case of a patient with severe cardiac disease taking stable maintenance doses of warfarin and amiodarone in whom the emergence of amiodarone-induced thyrotoxicosis was heralded by an abrupt increase in the prothrombin time.

(Woeber KA, Warner I. Potentiation of warfarin sodium by amiodarone-induced thyrotoxicosis. West J Med 1999; 170:49–51)

From the Department of Medicine, University of California, San Francisco (UCSF)/Mount Zion Medical Center, San Francisco, California.

Reprint requests to Kenneth A. Woeber, MD, FRCPE, UCSF/Mount Zion Medical Center, PO Box 1640, San Francisco, CA 94143-1640 (e-mail: woeber@itsa.ucsf.edu).

Report of a Case

The patient, a 73-year-old man, had coronary heart disease, severe left ventricular dysfunction, type 2 diabetes mellitus, systolic hypertension, and hypercholesterolemia. His course had been complicated by recurrent episodes of supraventricular tachycardia that resulted in acute pulmonary edema. Various antiarrhythmic drugs had been used in an attempt to control the episodes of supraventricular tachycardia, but only amiodarone was found to be effective. Accordingly, he had been taking amiodarone, 200 mg a day, for about two years without a recurrence of supraventricular tachycardia. During this period, he had also been taking warfarin to maintain an international normalized ratio (INR) of the prothrombin time of approximately 2.0. His other medications included losartan potassium, metoprolol tartrate, isosorbide mononitrate, furosemide, digoxin, aspirin, pravastatin sodium, and glyburide. On this regimen, he had felt relatively well, and his serum thyrotropin values were normal on numerous occasions, the most recent value being 1.7 mU per liter (normal, 0.4–5.5) in October 1996. He was taking a stable maintenance dose of 3.5 mg of warfarin sodium a day, and the doses of his other medications had not been changed nor had new medications been added.

In February 1997, the patient's INR abruptly increased to 5.5 (verified by repeat analysis), and the dose of warfarin was reduced to 2.5 mg a day (Table 1). In the ensuing two months, the patient noticed increasing effort intolerance, muscle weakness, fatigue, and weight loss without a change in appetite. He had no history of thyroid disease, and thyroperoxidase and thyroglobulin antibodies were absent in serum. He was not taking nonprescription drugs or nutritional supplements.

On examination, he weighed 67 kg (148 lb) and was 71 in tall, with a regular pulse of 90 beats per minute and a blood pressure of 150/70 mm Hg. Eye signs of thyrotoxicosis were absent. The thyroid gland was nontender and normal in size, but firmer than normal and with a finely irregular surface. An S_3 gallop and an apical systolic murmur were present. Breath sounds were decreased at both bases. There was no peripheral edema. The limb-girdle musculature was wasted, and a fine tremor of the hands was present.

ABBREVIATIONS USED IN TEXT
INR = international normalized ratio
RAIU = radioiodine uptake

Laboratory investigation elicited the following values: serum thyrotropin, less than 0.1 mU per liter; serum free thyroxine (T_4), 41 pmol per liter (normal, 9–20); and 24-hour thyroid radioiodine uptake (RAIU), less than 0.01 (normal, 0.12–0.30). A chest radiograph revealed worsening left ventricular failure. Results of liver function tests were normal.

A diagnosis of amiodarone-induced thyrotoxicosis was made that was substantiated by the markedly suppressed RAIU value. As amiodarone could not be discontinued because of concern about recurrent arrhythmia, the dose was reduced to 100 mg a day, and a regimen of methimazole, 30 mg a day, was begun. Potassium perchlorate, 200 mg a day, was added, as soon as it was obtained about two weeks later, to block thyroid iodide uptake.

Over the next two months, the patient's clinical condition steadily improved, and serum free T_4 values returned toward normal. Potassium perchlorate was discontinued, the dosage of methimazole was reduced to 20 mg a day, and later it was also discontinued. The decline in the serum free T_4 level was accompanied by a concordant decrease in warfarin sensitivity, expressed as the quotient of INR and warfarin dose (Table 1).

Discussion

Amiodarone and warfarin are often prescribed concurrently in the management of patients with cardiac tachyarrhythmias. Thyrotoxicosis induced by amiodarone use may appear at any time during administration of the drug and often does so abruptly. A cytotoxic effect of the drug may lead to thyroiditis, iodine release from the drug may lead to the Jod-Basedow phenomenon, or a combination of these effects may be responsible.[6] Although amiodarone may potentiate warfarin action by interfering with its metabolic disposition, our patient had been taking both drugs for two years before the relatively abrupt emergence of thyrotoxicosis that, in retrospect, was heralded by an increase in warfarin sensitivity. Accordingly, it is unlikely that the potentiation of warfarin action was due to amiodarone per se. Moreover, the doses of the other medications that the patient was taking had not been changed, and no new medications had been added that might have accounted for the potentiation of warfarin action. On the other hand, a close concordance was noted between the serum free T_4 level and warfarin sensitivity, expressed as the quotient of INR and warfarin dose, and this concordance was still evident when the serum free T_4 level was transiently subnormal as a result of treatment (Table 1).

The potentiation by thyrotoxicosis of the anticoagulant effect of warfarin has been reported from time to

TABLE 1.—*Warfarin Sensitivity in Thyrotoxicosis**

Date	*INR*	*Warfarin, mg/day†*	*INR:Warfarin Rotia*	*Free T_4 Level, pmol/liter*
12/26/96	1.9	3.5	0.54	—
1/24/97	1.8	3.5	0.51	—
2/24/97	5.5	3.5 (2.5)	1.57	
3/07/97	1.8	2.5 (3.0)	0.72	
3/21/97	2.0	3.0	0.67	—
4/22/97	3.2	3.0 (2.5)	1.07	
5/05/97	2.2	2.5	0.88	41
5/20/97‡	2.2	2.5	0.88	—
6/09/97§	2.0	2.5	0.80	40
6/23/97	2.1	2.5	0.84	28
7/14/97	1.6	2.5 (2.7)	0.64	22
7/28/97	1.5	2.7 (3.0)	0.56	18
8/11/97‖	1.7	3.0 (3.5)	0.57	15
9/12/97#	1.8	3.5	0.51	—
9/29/97	1.9	3.5	0.54	10
11/3/97¶	1.3	3.5	0.37	6
12/1/97	1.8	3.5 (4.0)	0.51	12
1/5/98	2.5	4.0	0.62	15

*INR = international normalized ratio, T_4 = thyroxine
†Values in parentheses refer to a subsequent dose adjustment.
‡Treatment with methimazole, 30 mg a day, was begun.
§Treatment with potassium perchlorate, 200 mg a day, was begun.
‖Methimazole dosage reduced to 20 mg a day and potassium perchlorate discontinued.
#Methimazole dosage reduced to 10 mg a day.
¶Methimazole discontinued.

time.[2–4] This apparent paradoxical effect, however, is not generally appreciated because the dosage requirements of most other drugs are increased in thyrotoxicosis as a result of increased degradation. Warfarin exerts its anticoagulant action by interfering with the activation of the four vitamin K–dependent clotting factors, II, VII, IX, and X, through the inhibition of vitamin K epoxide reductase. In thyrotoxicosis, the metabolic clearance rate of some of these factors is increased, and the concentration of factor II is depressed.[4,5] Thus, less warfarin would be required to prolong the prothrombin time in patients with thyrotoxicosis. In our patient, sensitivity to warfarin, which we have expressed as the quotient of INR and warfarin dose, increased abruptly when the patient first became aware of symptoms that, in retrospect, were in all likelihood due to the emergence of amiodarone-induced thyrotoxicosis. Return to the euthyroid state was accompanied by a decrease in sensitivity to warfarin.

REFERENCES

1. Kelly JG, O'Malley K. Clinical pharmacokinetics of oral anticoagulants. Clin Pharmacokinet 1979; 4:1–15

2. Vagenakis AG, Cote R, Miller ME, Braverman LE, Stohlman F Jr. Enhancement of warfarin-induced hypoprothrombinemia by thyrotoxicosis. Hopkins Med J 1972; 131:69–73

3. Self T, Weisburst M, Wooten E, Straughn A, Oliver J. Warfarin-induced hypoprothrombinemia: potentiation by hyperthyroidism. JAMA 1975; 231: 1165–1166

4. Kellett HA, Sawers SA, Boulton FE, Cholerton S, Park BK, Toft AD. Problems of anticoagulation with warfarin in hyperthyroidism. Q J Med 1986; 58:43–51

5. Shenfield GM. Influence of thyroid dysfunction on drug pharmacokinetics. Clin Pharmacokinet 1981; 6:275–297

6. Bartalena L, Brogioni S, Grasso L, Bogazzi F, Burelli A, Martino E. Treatment of amiodarone-induced thyrotoxicosis, a difficult challenge: results of a prospective study. J Clin Endocrinol Metab 1996; 81:2930–2933

Persistent Hiccups Induced by Dexamethasone

JAMES ROSS, BA
MOHSEN ELEDRISI, MD
PAUL CASNER, MD, PHD
El Paso, Texas

HICCUPS OR SINGULTUS are transient events experienced occasionally by most people. They are usually benign and of brief duration, but may become persistent. Although the cause of most episodes is never determined, many known associated conditions have been identified, including medications. We present a case of hiccups induced by the administration of dexamethasone.

(Ross J, Eledrisi M, Casner P. Persistent hiccups induced by dexamethasone. West J Med 1999; 170:51–52)

From the Department of Internal Medicine, Texas Tech University Health Science Center, El Paso, Texas.

Reprint requests to Mohsen Eledrisi, MD, Department of Internal Medicine, Texas Tech University Health Science Center, 4800 Alberta Ave, El Paso, TX 79905 (e-mail: medemse@ttuhsc.edu).

Report of a Case

The patient, a 30-year-old man with no relevant medical history, presented with coffee-ground emesis on the day of admission and persistent hiccups for two days. He had recently been evaluated by a dermatologist in Mexico and had received 16 mg of dexamethasone intravenously for "allergic skin lesions." Unfortunately, no further information was available. He denied prior intake of any medications, alcohol, or tobacco.

A physical examination showed persistent hiccups at a rate of 6 to 9 per minute, mild epigastric tenderness, and heme-positive stools. Multiple circumscribed papular skin lesions were seen over the flexor surface of the upper extremities, consistent with urticaria. Laboratory evaluation revealed a leukocyte count of 17.27×10^9 per liter with a normal differential cell count, a hemoglobin level of 158 grams per liter, and a hematocrit of 0.45. The results of electrolyte tests, liver function tests, and coagulation studies were normal.

Esophagogastroduodenoscopy revealed erosive esophagitis and gastritis. The following techniques were attempted unsuccessfully to terminate hiccups in the patient: Valsalva maneuver, stimulation of the pharynx with a cotton-tipped swab, and drinking water. The patient continued to have hiccups that also failed to respond to treatment with chlorpromazine.

The patient's hiccups resolved four days after the initial dexamethasone injection. Because dexamethasone was suspected as the cause of hiccups, the patient was offered a challenge test. The benefits and risks were explained to him, specifically the identification of a possibly avoidable drug side effect. After his authorization, the same dose of dexamethasone was administered intravenously one week after his discharge from the hospital. His hiccups reappeared within two hours and disappeared after 36 hours.

Discussion

Hiccups are involuntary contractions of the diaphragm, terminated by the abrupt closure of the glottis. Transient hiccup episodes can last as long as 48 hours. When an episode continues for more than 48 hours, it is termed persistent. Hiccups lasting longer than one month are considered intractable.[1] Transient hiccups occur equally in both sexes, but persistent and intractable hiccups occur more frequently in men.[2] Hiccups serve no physiologic function. The physiologic mechanism of hiccups is thought to result from the stimulation of one or more of the three components of the hiccup reflex arc, the afferent, central, and efferent limbs.[3] The afferent limb comprises the phrenic and vagus nerves and the sympathetic chain from thoracic segments T6 to T12. The central connection between the afferent and efferent limbs is attributed to a nonspecific anatomic location between cervical segments C3 and C5. The efferent limb consists primarily of the phrenic nerve, in addition to the glottis, accessory respiratory muscles, and a complex interaction between the brainstem and midbrain areas, including the

respiratory center, phrenic nerve nuclei, medullary reticular formation, and hypothalamus.

The evaluation of persistent and intractable hiccups should focus on a thorough history, physical examination, and laboratory studies necessary to disclose possible underlying causes that could stimulate this reflex. Medications are not considered a common cause of hiccups. Souadjian and Cain[2] in their review of 220 cases of intractable hiccups do not report medications as a cause. Only three cases of dexamethasone-induced hiccups were reported in the literature.[4–6] In another report, hiccups were associated with dexamethasone-cyclophosphamide pulse therapy.[7] Persistent hiccups have also been reported with the use of methylprednisolone.[8]

The mechanism of corticosteroid-induced hiccups is not known. It has been proposed that corticosteroids may stimulate the hiccup reflex arc. Animal studies suggested that corticosteroids reduce the synaptic transmission threshold in the midbrain.[9]

The incidence of corticosteroid-associated hiccups is unknown. The few cases reported indicate either that the incidence is low or that the effect is so mild and self-limited that it goes unrecognized. Discontinuing the suspected drug usually results in the termination of hiccups. Recovery may take several hours to a few days.

Because corticosteroids are widely used in medicine, we would like to raise the level of awareness among clinicians of the association between corticosteroids and hiccups. A drug history should be carefully reviewed as a possible cause of hiccups. This will obviate the need for further unnecessary investigations.

Acknowledgment

Manuel Rivera, MD, thoughtfully reviewed this report in manuscript form.

REFERENCES

1. Kolodzik PW, Eilers MA. Hiccups (singultus): review and approach to management. Ann Emerg Med 1991; 20:565–573

2. Souadjian JV, Cain JC. Intractable hiccup: etiologic factors in 220 cases. Postgrad Med 1968; 43:72–77

3. Lewis JH. Hiccups: causes and cures. J Clin Gastroenterol 1985; 7:539–552

4. LeWitt PA, Barton NW, Posner JB. Hiccups with dexamethasone therapy [letter]. Ann Neurol 1982; 12:405–406

5. Vazquez JJ. Persistent hiccups as a side effect of dexamethasone treatment [letter]. Hum Exp Toxicol 1993; 12:52

6. Cersosimo RJ, Brophy MT. Hiccups with high-dose dexamethasone administration: a case report. Cancer 1998; 82:412–414

7. Kanwar AJ, Kaur S, Dhar S, Ghosh S. Hiccups—a side-effect of pulse therapy [letter]. Dermatology 1993; 187:279

8. Baethge BA, Lidsky MD. Intractable hiccups associated with high-dose intravenous methylprednisolone therapy. Ann Intern Med 1986; 104:58–59

9. Feldman S, Todt JC, Porter RW. Effect of adrenocortical hormones on evoked potentials in the brain stem. Neurology 1961; 11:109–115

Lessons From the Practice

Alone

WILLIAM E. BYRD, MD, *Roanoke Rapids, North Carolina*

Loneliness is not the sickness unto death. No, but can it be cured except by death? And does it not become the harder to bear the closer one comes to death?

Markings, 1966
DAG HAMMARSKJOLD

Two weeks after I entered private practice, I met a man whose quick and unlamented departure from this world would create a lasting impression on my mind.

At 7 PM on Thanksgiving evening, I was called to the emergency department to see a 63-year-old man who had sustained a massive anterior myocardial infarction. Mr Evans,* an unemployed plumber, developed severe chest pain after leaving a local Mexican restaurant. A rescue squad was quickly summoned, and he was transported to our hospital emergency department, where he was found to be hypotensive and in complete heart block. After thrombolytic therapy was initiated and a temporary pacemaker inserted by the cardiologist on call, he was then transferred to the coronary care unit. As soon as nurses had adjusted the oxygen and intravenous fluids, I introduced myself and began to take his history. Despite his precarious state, Mr Evans was pleasant and courteous, continually thanking the physicians and nurses for their care.

He was slender, muscular, 5'9" tall, and weighed about 68 kg (150 lb). He was clean-shaven and appeared to be somewhat younger than his stated age. A brief history revealed that he was a widower of 20 years and had a son and daughter living in a neighboring state. At his request, the nurse removed a worn calling card, "Bob's Plumbing and Air Conditioning," from his wallet. On the back were scrawled two names—Sandra and Mark—with corresponding telephone numbers.

Looking at me, he said, "You can call my children, if you like."

"I'll be happy to," I responded.

By this time, Mr Evans was experiencing more chest pain, requiring both intravenous nitroglycerin and morphine sulfate. His blood pressure was barely holding at 90 mm Hg systolic, despite a dopamine hydrochloride drip. His electrocardiogram revealed diffuse ST elevation in the anterior and precordial leads, all compatible with an anterior myocardial infarction with extension. With the patient in impending cardiogenic shock, I realized I needed to notify the children immediately to give them sufficient time to arrive before their father's condition deteriorated further.

I decided to call the son first. The phone was picked up on the second ring. The background was filled with laughter and the clinking of glasses.

"May I speak with Mark Evans, please?" I asked.

"I'm your man, buddy," a jovial voice responded.

I introduced myself and told him of his father's critical condition. After I finished, there was a long silence. I thought I had been disconnected.

"Hello, Mr Evans? Hello?" I repeated.

"I hear you," Mark Evans replied, speaking without emotion.

I continued, "Your father may die within the next 24 hours, so I thought you might wish to get down and see him if you can."

There was another minute of complete silence, and then, "He was no father to me."

"I see," I said, taken aback. "Then, what do you want me to tell him?"

"I really don't give a damn what you tell him, Doc," Mark Evans replied, the decibels of his voice increasing severalfold.

Collecting myself, I said, "If he should die in the next few hours, do you wish me to call you?"

"Not particularly," he said. "Don't they have ways of disposing of bodies that no one claims?" I then began breathing deeply, feeling chilled all over. I had never encountered such a situation either in residency or fellowship training. I was trying to think how best to respond.

Speaking slowly, I said, "I believe the coroner can cremate an unclaimed body."

"Then cremate the son-of-a-bitch!" he screamed. With that, he hung up.

With the phone quivering in my hand, I clenched my teeth for a moment, waiting for the ringing in my ears to stop. Shaking my head several times, I then dialed the daughter's number. The phone was immediately

*This patient vignette has been modified to protect the identity of the patient and the family.

(Byrd WE. Alone. West J Med 1999; 170:53–54)

Dr Byrd is in private practice at Roanoke Valley Internal Medicine and Rheumatology in Roanoke Rapids, North Carolina.
Reprint requests to William E. Byrd, MD, 1724 E 10th St, PO Box 1093, Roanoke Rapids, NC 27870.

answered. I introduced myself and said, "Is this Sandra Evans, the daughter of Robert Evans?"

"I'm Sandra Martin now," a cold voice replied.

I then proceeded to tell her about her father's near-terminal condition. Concluding, I said, "Your father asked if you would be coming in the next several hours."

There was no response. After about a minute, she said, "I think I'll pass on this one. Why don't you call my brother."

"I have," I responded.

"And?"

"He said he wouldn't be able to make it either."

Laughing, she said, "I guess not. Probably car trouble." After pausing for an additional moment, she continued, "Unbelievable. After 20 years."

"I beg your pardon?" I said.

"Oh, nothing," she replied. Her voice now becoming icy, she responded, "I've really got to go now—bridge party, you know. You sound tired, Doctor. Why don't you just get some sleep and let nature take its course." Before I could answer, she hung up.

Sitting down, I pondered how best to approach Mr Evans. When I returned to his room, he was pale and lethargic, with his blood pressure now 60/0 mm Hg. As I spoke to him, he seemed to rally briefly, smiling and waiting for me to respond. He then asked, "Did you get them?"

"Yes, I did. I talked to them both."

"Are they coming?"

Hesitating a second, I said, "They're on their way." He then exhaled deeply and fell back on his pillow.

I stepped out of the room to go to the nursing station, when both nurses jumped up shouting, "Code Blue! Code Blue, room 3!" The next few moments were pandemonium, with crash carts, nurses, and anesthetists rushing into room 3. Mr Evans was in asystole, and cardiopulmonary resuscitation was continued for about 15 minutes. It was to no avail, and he was pronounced dead.

As I left the coronary care unit, my shirt drenched with sweat, I headed for the on-call room to get a shower. I slept fitfully the rest of the night, despite the fact that I received no calls from the emergency department. The next morning, as I checked out with the oncoming physician, I asked him to call me if he heard anything from the family. There were no calls, and I returned to my daily routine at the office.

Three weeks later, I decided to call the coroner's office to see who had claimed Mr Evans' remains. Wilson Askew, the coroner, quickly responded, "Oh, yes. Evans, poor fellow. No one claimed the body. Not so much as a phone call. We cremated him last Friday."

As I hung up, I felt I had participated in some type of pagan ritual. What could Robert Evans have possibly done to his children to merit such treatment—such complete suspension of human decency? I would never know. But would it have really made a difference if I had known? Probably not. I had missed the first several acts of his life and had witnessed only the final, tragic scene in a lifelong drama.

* * *

"Lessons From the Practice" presents a personal experience of practicing physicians, residents, and medical students that made a lasting impression on the author. These pieces will speak to the art of medicine and to the primary goals of medical practice—to heal and to care for others. Physicians interested in contributing to the series are encouraged to submit their "lessons" to the series' editors.

Saying No

VICTORIA MAIZES, MD, *Tucson, Arizona*

Saying no to patients is not something that most physicians learn in medical school. Nor does it come naturally or instinctively. Rather, after years of trial and error, as patients ask for things that physicians consider inappropriate, physicians eventually develop a style that works for them.

How patients feel about their physicians' saying no is another matter. No one likes to be told no. When physicians say no, patients often don't return. They perceive themselves in a "one-down" situation. They may feel embarrassed and look for another physician.

The specific situations are familiar ones. Whether the patient is asking for a third or fourth refill of Vicodin (combination product of hydrocodone bitartrate and acetaminophen) for chronic back pain, wants to be classified "disabled" for a problem that seems minor, or is convinced that magnetic resonance imaging is the only thing that will answer his or her questions, physicians have often heard these requests before. The automatic response often is to lecture the patient on why the request is not a good idea.

Yet, even as physicians say no, they struggle with it. There is often uncertainty in medical situations. One way to handle uncertainty is to trust the patients. Physicians want to be liked. Finally, saying no takes longer (at least initially) than "giving in" and granting patients their requests. But if physicians give in, they then feel compromised.

When searching the literature to prepare this article, I was surprised to find that nothing had been written on the topic. I questioned colleagues, who concurred. Yet, interest among practicing physicians is high. Managed care's quarterly member-satisfaction surveys give physicians an incentive to improve their communication skills. A "No" said without finesse often leads to a patient complaint, another item tracked by many health maintenance organizations.

As a brief negotiation trainer,* I repeatedly heard the question, "What about when you have to say no?" In a series of focus groups, I developed and tested the following seven steps and found them effective in preserving the physician-patient relationship.

*Brief negotiation is a communication skill that clinicians use to increase patient motivation to make lifestyle changes.

Step 1. Listen

Make sure you clearly understand what the patient is asking for. A patient's request for a magnetic resonance imaging scan may be a request for a more specific diagnosis.

Draw the patient out with encouraging comments like "Tell me more." This is counterintuitive because the physician's initial impulse usually is to try to stop the patient from talking.

Step 2. Acknowledge

Restate your patient's request so he or she knows you've heard and understood the request.

Use reflective listening. For example, in response to a patient's request for diet pills, reflect back: "What I hear you saying is, you really want to lose weight," or, in response to a request for pain medication: "You really want to reduce your pain." It is important not to trivialize the patient's experience.

Step 3. Preamble

Develop your own introduction. For example: "I know this is something you were really hoping I could help you with," or "This is really difficult for me to say."

Step 4. Express Empathy

Empathy toward the patient needs to be genuine. Consider how you felt when an authority figure refused one of your requests.

Find your own language. For example: "I care about you; I would like to work with you to try to find a solution."

Step 5. Explain Rationale

Your patient may or may not be willing to hear your rationale (due to anger, frustration, and so forth). Summarize your reason briefly, using terms that are clear, plain English, not medical jargon.

(Maizes V. Saying no. West J Med 1999; 170:55–56)

From the Program in Integrative Medicine, The University of Arizona Health Sciences Center, Tucson, Arizona.
Reprint request to Victoria Maizes, MD, Program in Integrative Medicine, PO Box 245153, Tucson, AZ 85724 (e-mail: vmaizes@ahsc.arizona.edu).

Ask permission before giving a longer explanation. "Do you want to know more?"

Use "I" language. For example: "I don't prescribe Vicodin for chronic pain because I find . . .," not "You shouldn't use Vicodin because you may become addicted."

Step 6. Ask for a Response

Requesting a response from the patient helps assess whether the patient has understood your perspective. "Do you understand why I can't . . ?" Listen to the answer.

Step 7. Assess Readiness to Consider Other Options

Ask the patient, "Would you be interested in exploring other options?" If the patient is not ready, don't push other options.

These seven steps help protect the therapeutic relationship with patients when physicians must say no. They need not be followed sequentially, and the spirit in which they are communicated is undoubtedly more important than the actual words. Although they cannot ensure that every patient visit ends on a positive note, they are likely to help.

* * *

"Lessons From the Practice" presents a personal experience of practicing physicians, residents, and medical students that made a lasting impression on the author. These pieces will speak to the art of medicine and to the primary goals of medical practice—to heal and to care for others. Physicians interested in contributing to the series are encouraged to submit their "lessons" to the series' editors.

JONATHAN E. RODNICK, MD
STEPHEN J. MCPHEE, MD
Assistant Editors

Poetry

* * *

As I Looked Again

The photograph:
Oakland, California,
History Room; 1918 flu
epidemic; auditorium
filled with cots of people
dying! Crosscurrents
in memory...
a little girl running
our farm's meadow like
a young doe wide-eyed
startled wonderment;
eyes flooded, dark-
ringed in Argyrol,
keep flu away!

Leaning into the photograph,
swift heartbeat, the story came...
Philadelphia; my 18-year-old
cousin, hopping his bike,
delivering, door to door,
the corner druggist's medicines;
home, exhausted to bed,
doctor said, *Too late.*
He's gone. Flu, three days, dead!
1997: photograph "in time," emotion
feeling his dark curly hair
neatly arranged over a passive,
pale face, movement of the glide
into death, mine.

Esther Buffler
Portsmouth, New Hampshire

Photo Courtesy of the Historical Photograph Collection of the Oakland Public Library, Oakland, California.

Classified Advertisements

The rate for each insertion is **$1.50 per word, with a 30 word ($45) minimum.** Confidential box number charge: $10 each month.
A word is defined as one or more letters bounded by spaces. The following gives some examples:

Linda H. Clever, MD	= 4 words	allergy/immunology	= 1 word
Send CV	= 2 words	Sacramento, CA 95817	= 3 words
A	= 1 word	804-979-8034	= 1 word
February 22, 1997	= 3 words		

Classified display rate $70 per inch. Maximum sizes: 1 column by 5" or 2 columns by 2" (2-1/8" per column). Larger classified ad space by special arrangements.
Copy for classified advertisements should be received not later than **first of the month preceding issue. All copy must be typed or printed.** Classified advertisers using Box Numbers forbid the disclosure of their identity; your inquiries in writing will be forwarded to Box Number advertisers. Although *The Western Journal of Medicine* believes the classified advertisements in these columns to be from reputable sources, we do not investigate the offers made and assume no liability concerning them. The right is reserved to reject, withdraw, or modify all classified advertising copy in conformity with the decisions of the Advertising Committee.

Please Type or Print Advertising Copy

Classified Advertisements Are Payable in Advance
CLASSIFIED ADVERTISEMENTS, THE WESTERN JOURNAL OF MEDICINE
221 MAIN STREET, SAN FRANCISCO, CA 94120-7690
(415) 882-5177; FAX (415) 882-3379
Ads may be placed online at www.wjmed.com

PHYSICIANS WANTED

PHYSICIAN Outpatient Clinic. The County of San Mateo has an immediate opening for a Board certified/eligible physician for our new South San Francisco clinic opening in April 1999. Two years experience providing primary care services to a predominantly adult population. Spanish speaking preferred. Full-time position with excellent benefits and competitive salary. Fax CV to (650) 573-2458, or mail to 455 County Center, Redwood City, CA 94063. EOE. COUNTY OF SAN MATEO

ASSISTANT or ASSOCIATE PROFESSOR, DIVISION OF NEPHROLOGY. The University of California, Davis, School of Medicine, Department of Internal Medicine is recruiting a full-time Assistant or Associate Professor. The position requires demonstrated leadership abilities in the subspecialty, strong clinical skills, excellence in teaching. Candidates must be Board certified in Internal Medicine and Board eligible or Board certified in the subspecialty of Nephrology. Please forward Curriculum to: George Kaysen, M.D., Ph.D., c/o Julie Mustard, Department of Internal Medicine, University of California, Davis, 4150 V Street, 3100 PSSB, Sacramento, CA 95817. This position is open until filled but no later than February 28, 1999. The University of California is an affirmative action/equal opportunity employer.

California Department of Corrections

Health Care Services Division

As one of the largest, most unique and stable employers of mental health care professionals, we currently have administrative opportunities at various locations for California Licensed Physicians.

CHIEF PSYCHIATRISTS
In these lead positions, your prior supervisory and administrative experience are a definite asset. You will direct and manage our collegial team of Mental Health professionals in one of the following locations: Pelican Bay State Prison, Crescent City; Central California Women's Facility, Chowchilla; California Substance Abuse Treatment Facility and State Prison, Corcoran; Salinas Valley State Prison, Soledad; California State Prison Lancaster; North Kern State Prison, Delano; Wasco State Prison, Wasco; California State Prison, Vacaville; California Institution for Men, Chino; and High Desert State Prison, Susanville.

CHIEF MEDICAL OFFICER
You will be responsible for the management & quality assurance of the Medical Program; Pharmacy; Medical Records and Dentistry; and must be licensed to practice in California. Current opportunities are at Salinas Valley State Prison, Soledad near the beautiful Monterey Peninsula; and in the far Northern Region of California at High Desert State Prison, Susanville in Lassen County.

Our generous benefit plan includes medical/dental/vision plan, competitive salary, safety retirement and more. Contact Medical Recruiter, Health Care Services Division, P.O. Box 942883, Sacramento, CA 94283-0001. Phone: 916-327-7081. Fax: 916-327-1436. Online: www.spb.co.gov. EOE.

HEALTH CARE SERVICES DIVISION
CALIFORNIA DEPARTMENT OF CORRECTIONS
PUBLIC SAFETY. PUBLIC SERVICE

1/99

Defining the future of healthcare

Take a closer look at the future of healthcare, a future taking shape at The Cleveland Clinic Foundation. We have built the region's largest and most prestigious healthcare organization through a commitment to international leadership and top quality patient care, education and research.

The recent partnership between The Cleveland Clinic and the Wooster Clinic has created excellent opportunities for Board Certified/Eligible:

Internists • Cardiologists
Pulmonologists • Gastroenterologists

Enjoy the advantages of practicing personalized, community-based medicine combined with access to state-of-the-art facilities at The Cleveland Clinic's main campus. The Wooster, Ohio location offers a wonderful, family-oriented community, in a progressive college town. Become part of an expanding, multispecialty medical group.

Qualified professionals will receive a competitive salary, excellent benefits and paid meeting and vacation time. Send curriculum vitae to: **Attn: John Ferkan, Manager, Physician Recruitment, The Cleveland Clinic Foundation, P.O. Box #606140, Cleveland, OH 44106. Fax: 216-738-4059. email: ferkanj@cesmtp.ccf.org.** We are proud to be an equal opportunity employer. Smoke/drug-free environment.

Visit our homepage on the world wide web: **www.ccf.org.**

THE CLEVELAND CLINIC
Every Life Deserves World Class Care

PHYSICIANS WANTED

Physician needed part-time (.2–.5 FTE) to provide geriatric primary care and some adult internal medicine for our *Over 60 Health Center* in East Oakland. Board Certification IM or FP required. Community clinic/minority background experience highly desirable. Contact: Dr. Floyd Huen, Medical Director (510) 597-8010 Ext. 407. Resume: LifeLong Medical Care, 1860 Alcatraz Avenue, Berkeley, CA 94703.

YELLOWSTONE NATIONAL PARK. Physician to cover outpatient clinic, emergency room, and inpatient at Lake Hospital from May to September 1999. Send CV to: Yellowstone Park Medical Services, 707 Sheridan Avenue, Cody, WY 82414 or call 1-800-654-9447 (ext. 462).

PSYCHIATRIST

Full time position in central California; convenient to San Francisco, Lake Tahoe & West coast. Working with large community mental health program with UC Davis link; Adult Outpatient; no call; advanced multi-disciplinary team. Please call Kathy Lopez, Human Resources; or Randall Stenson, M.D.; or Roger Speed, Director, at:

(209) 468-8750

IDAHO

Make One Of America's Best Places to Live Even Better.

Where You'll Work.
Primary Health, Idaho's largest, fastest-growing integrated health care system whose network of family medicine immediate care centers, by-appointment family practitioners, pediatricians and OB/GYNs serves beautiful southern Idaho.

Where You'll Live.
In a great place to raise a family with quality schools, incredible outdoor recreation and a rural atmosphere close to a metropolitan area with a beautiful performing arts center, excellent hospitals and professional sports.

What You'll Get.
The financial backing and medical resources of a major health care network. A competitive salary, ownership options, flexible work and call schedules, professional growth, full benefits including medical and dental and much more.

Submit CV and questions to:
BECKY NELSON
(800) 688-5008 ext. 507 • FAX (208) 344-4262
Physician Recruitment
800 Park Boulevard, Suite 760
Boise, Idaho 83712

Primary Health

ADVERTISING INDEX

eBMJ . . . . . 2nd Cover
BMJ REPRINTS . . . . . 3rd Cover
STUDENT BMJ . . . . . 4th Cover
J MED ETHICS ORDER FORM . . . Page 63
BMJ QUALITY IMPROVEMENT CONFERENCE . . . . . Page 64

Reprints

Any article printed in *WJM* can be purchased in quantities of 100 or more. Printed on fine quality journal stock. Prices are based upon article length and quantity ordered.

Contact Marsha Fogler, Medical Reprint Services, PO Box 3227, Cherry Hill, NJ 08034
Phone (800) 482-1450;
Fax (609) 482-7414;
E-Mail: fogler@erols.com

The California Academy of Family Physicians invites you to attend our 51st Annual Scientific Assembly February 12-14, 1999 in Beautiful San Diego

Featuring:

- A keynote address by Nancy Dickey, MD, President of the American Medical Association & Family Physician
- 9 clinical lectures on a wide array of topics
- 4 procedural workshops
- 5 practice management/clinical seminars
- An unforgettable drama about teen health concerns
- Panel discussion on implications of genetic testing
- 6 interactive, open discussion forums
- Preconference Internet and Smart Coding seminars
- 9 satellite CME Sessions at no additional cost

Receive up to 43.5 hours of CME Credit

Outstanding Workshops & Seminars

CALIFORNIA ACADEMY OF FAMILY PHYSICIANS

For details and registration info, call 415-394-9121
Or — register online at www.FamilyDocs.org/Register

INSTRUCTIONS FOR AUTHORS

In accordance with the Uniform Requirements for Manuscripts Submitted to Biomedical Journals (URM), 1997

Our readers represent all branches of medicine. We wish to receive and publish manuscripts that are reliable and lively and that will improve the care of patients, the health of the public, or policies affecting either. Manuscripts should be of interest to a broad range of scholars, busy practitioners, students, and physicians in training who have a clinical orientation. The purpose of a paper or letter may be to report, inform, alert, review, and discuss, but, above all, to teach. Titles should be short and intriguing. Avoid the overuse of jargon, adverbs, and expendable words and phrases; use only standard abbreviations and acronyms; and use inclusive language (see AMA Manual of Style, 8th Edition). We appreciate your interest in The Western Journal of Medicine and our profession.

Manuscript Information

Manuscripts should be sent to the Editor, Linda Hawes Clever, MD, c/o Publisher, The Western Journal of Medicine, 221 Main Street, San Francisco, CA 94120-7690. Manuscripts must be original, not previously published, and not under consideration by another publisher. If preliminary data were included in another presentation or publication, this should be noted in the cover letter, and a copy of that publication should be included. Any conflict of interest, actual or potential, should be revealed to the Editors (see Letter of Transmittal). Obtaining informed consent to protect patients' rights to privacy should be documented according to URM 1997.

All manuscripts should be double-spaced and, including references and abstract but not tables, should not exceed:

- Articles: 3,000 words (15 double-spaced pages)
- Conferences and Reviews: 3,000 words
- Topics in Primary Care Medicine: 3,000 words
- Case Reports, Alerts, and Notices: 1,500 words
- Commentaries: 2,000 words
- Lessons From the Practice: 1,000 words
- Letters to the Editor: 500 words
- Epitomes: 800 words

Manuscripts, except for Case Reports, Epitomes, and Lessons From the Practice, should include a nonstructured abstract of no more than 150–200 words summarizing the article. Abstracts should include a description of the purpose, design, patients, results, and conclusions.

Letters to the Editor must be double-spaced and will be published at the discretion of the Editors. They may be edited for style and brevity. Those of a scientific nature may be subject to peer review. They should be no more than 500 words in length. Authors will be sent page proofs before publication.

All manuscripts will be subject to peer review in addition to review by the Editors to determine the originality, validity, and importance of content and conclusions. Reviewers' comments will be returned with rejected manuscripts at the discretion of the Editors. All reviewers will remain anonymous but will be required to state possible conflicts of interest.

All accepted manuscripts are subject to copyediting, and the corresponding author is sent edited page proofs for approval and necessary minor changes. Excessive changes at this stage may result in a delay of publication or withdrawal of the paper. No changes will be made after the final, edited version has been approved by the corresponding author without notifying the author. It is the corresponding author's responsibility to clear all corrections and changes with coauthors.

Letter of Transmittal

All authors must sign the letter of transmittal, with one author designated as correspondent and his or her name, address, and telephone and fax numbers included.

The order of authorship is determined by the authors. All authors should meet the basic criteria for authorship (as stated below). Because the order of authorship is assigned in different ways, its meaning cannot be inferred accurately unless it is stated by the authors. Authors may explain the order of authorship in a footnote.

A letter of transmittal, except for one accompanying a manuscript from US Government employees whose work was done as part of their official duties, must include a paragraph that transfers copyright: "In consideration for reviewing and editing my submission, the author(s) undersigned hereby transfers, assigns, or otherwise conveys all copyright ownership to The Western Journal of Medicine, in the event that such work is published by the journal."

The letter of transmittal must include a statement of author responsibility signed by all authors: "I have participated in the conception and design of this work and in the writing of the manuscript and take public responsibility for it. I have reviewed the final version of the manuscript and approve it for publication. I attest to the validity and legitimacy of data in the manuscript and agree to be named as the lead author or coauthor of the manuscript."

The letter of transmittal must include a description of sources of funding and the role of sponsors, including their involvement, if any, in review and approval of the manuscript for publication. The letter must also include a statement of financial disclosure: "I warrant that I have no financial interest in the drugs, devices, or procedures described in the enclosed manuscript (except as disclosed in the attached statement)."

Research or project support should be included as a footnote to the manuscript or in the accompanying cover letter.

Manuscripts concerned with experimental investigation on human subjects must include in the text a statement that all subjects gave their informed consent and that approval was obtained from the appropriate ethics committee.

Acknowledgments will be printed on a select basis—to acknowledge those who contributed to but were not involved in the writing or review of the paper. They should not include persons whose work on the manuscript was a part of their regular duties.

Preparation of Manuscripts

Everything, including references, tables, figure legends, and abstracts, must be double-spaced.

Please submit the following: The original manuscript, two copies, and a copy of the manuscript on disk (labeled with the word processing program used). Allow a margin of 2.5 to 4 cm (1 to 1.5 in) on both sides. Be sure to include the references, tables, and figure legends on the disk. Formatting should be kept to a minimum. Manuscripts transmitted by facsimile machine are not acceptable unless requested by the Editors.

All values should be in Systeme International (SI) units, with metric equivalents following in parentheses. Temperature readings should be given in Celsius. Use the generic name of drugs, with the salt or ester given at the initial mention of a drug.

Figures (illustrations) should be submitted in triplicate in black and white, unmounted 12.7 X 17.8 cm (5 X 7 in) glossy prints, with the figure number, lead author's name, and top of the photo indicated with a label on the back. Patients (and relatives) have a right to anonymity in published clinical documentation. Details that might identify patients should be avoided unless essential for scientific purposes. Masking of the eye region in photographs of patients may be inadequate protection of anonymity. If identification of patients is unavoidable, informed consent should be obtained. This should be clearly stated and proof submitted with the manuscript. Changing the data on patients should not be used as a way of securing anonymity.

Figure legends, to be typed in sequence on the same page, should be in complete sentences. Any figures or tables previously published must be accompanied by a letter of permission to borrow from the copyright holder (the previous publisher). The permission of the authors should also be obtained. The Editors discourage the use of borrowed figures or tables.

Reprints

A form for ordering reprints will be sent to the corresponding author when the article is published.

References

All references should be cited in the text using superscript numbers and listed in their order of citation. They should be pertinent to the text and not simply a listing of the results of a computerized search. They should be in URM style according to the following examples. Do not use op cit or ibid.

References should be medical, scientific, or scholarly publications. Others—such as newspapers or magazines—should be kept to a minimum.

Journal Articles

Abbreviations of journal titles should conform to those used in Index Medicus. List up to six authors; for seven or more, use et al after listing the first six.

1. Vega KJ, Pina I, Krevsky B. Heart transplantation is associated with an increased risk for pancreatobiliary disease. Ann Intern Med 1996; 124:980–983

2. Parkin DM, Clayton D, Black RJ, Masuyer E, Friedl HP, Ivanov E, et al. Childhood leukaemia in Europe after Chernobyl: 5 year follow-up. Br J Cancer 1996; 73:1006–1012

No author given:

3. Cancer in South Africa [editorial]. S Afr Med J 1994; 84(12):15

Books

4. Ringsven MK, Bond D. Gerontology and Leadership Skills for Nurses. 2nd ed. Albany (NY): Delmar Publishers; 1996 [author of book is same as author of chapter]

5. Phillips SJ, Whisnant JP. Hypertension and Stroke. In Laragh JH, Brenner BM (Eds): Hypertension: Pathophysiology, Diagnosis, and Management. 2nd ed. New York: Raven Press; 1995, pp 465–478 [authors of book differ from chapter author]

Correspondence

6. Shusterman D. Espresso maker's wrist [correspondence]. West J Med 1990; 152:721–722

Scientific or Technical Report

Issued by funding or sponsoring agency:

7. Smith P, Golladay K. Payment for durable medical equipment billed during skilled nursing facility stays. Final report. Dallas (TX): Dept of Health and Human Services (US), Office of Evaluation and Inspections; 1994 Oct. Report No.: HHSIGOEI69200860

Issued by performing agency:

8. Field MJ, Tranquada RE, Feasley JC, editors. Health services research: work force and educational issues. Washington DC: National Academy Press; 1995. Contract No.: AHCPR282942008. Sponsored by the Agency for Health Care Policy and Research

9. Centers for Disease Control and Prevention. Recommendations and Reports: 1997 Revised guidelines for performing CD4+ T-cell determinations in persons infected with human immunodeficiency virus (HIV) MMWR 1997; 46(Jan 10):RR-2

Proceedings

10. Kimura J, Shibasaki H, editors. Recent advances in clinical neurophysiology. Proceedings of the 10th

International Congress of EMG and Clinical Neurophysiology; 1995 Oct 15–19; Kyoto, Japan. Amsterdam: Elsevier; 1996

Mass Circulation Publications

11. Lee G. Hospitalizations tied to ozone pollution: study estimates 50,000 admissions annually. The Washington Post 1996 Jun 21; Sect A:3 (col 5)

Personal Communications and Unpublished Data

The use of "personal communication" or "unpublished data" should be avoided and should not be included in the reference list. If such a notation provides essential information not available from a public source, it should be given in parentheses in the body of the text, listing the person's name, highest academic degrees, and professional affiliation, whether the communication was oral or written, and the date (month and year):
12. Lyme disease has been reported in red squirrels (J. Sneed, PhD, Department of Wildlife, written communication, September 1990).

For Further Information

Questions regarding the Instructions for Authors may be directed to the Editorial Manager, Catherine Nancarrow, *The Western Journal of Medicine*, 221 Main Street, San Francisco, CA 94120-7690. Telephone (415) 882-5177, Fax (415) 882-3379.

AUTHOR CHECKLIST

- ✓ Original manuscript and 2 copies; diskette.
- ✓ Everything double-spaced.
- ✓ Illustrations, black and white glossy, identified with lead author's name—3 sets, plus figure legends that describe fully and in complete sentences what the figure depicts.
- ✓ Letter of transmittal that includes release of copyright, statement of conflict of interest, funding source(s), and authorship responsibility, signed by all the authors.
- ✓ A 200-word unstructured abstract.
- ✓ Title page that includes current affiliation of all authors and an address and telephone and fax number for corresponding author.
- ✓ Permission-to-borrow letters for any previously published illustrations or tables.
- ✓ All references numbered consecutively, double-spaced, in URM style, and cited in text. No unpublished data or nonscientific publications listed in references (include in text).
- ✓ Informed consent obtained.

PUBLISHED BIMONTHLY

BMJ Publishing Group

JOURNAL OF

Medical

ETHICS

Journal of the Institute of Medical Ethics

Editor: Raanan Gillon

First published in 1975, *Journal of Medical Ethics* is a leading international journal featuring interdisciplinary articles on ethical aspects of health care. With an increase in frequency from quarterly to bimonthly, the journal offers original articles, case conferences, editorials, book reviews, correspondence, news and notes.

A Selection of Recent Papers:

"Goodbye Dolly?" The ethics of human cloning
John Harris

At the coalface - medical ethics in practice: First, do no harm
Scott Groudine and Philip D Lumb

Patients' rights in England and the United States of America: The Patients's Charter and the New Jersey Patient Bill of Rights: a comparison
Melanie H Wilson Silver

Subscription Rates

Institutional: Worldwide £132, USA Only $214

Personal: Worldwide £90, USA Only $146

Student Rate: Worldwide £47, USA Only $76*

* (Please send proof of student status)

VISIT OUR HOMEPAGE ON: **www.jmedethics.com**

ORDER FORM

Journal of Medical Ethics

ISSN 0306 6800 Publication: Bimonthly
1999 Subscription Rate: Institutional: Worldwide £132, USA Only $214
Personal Rate: Worldwide £90, USA Only $146
Student Rate: Worldwide £47, USA Only $76*
***(Please send proof of student status)**

☐ Send me instructions to Authors

☐ Send me a free sample copy

☐ Enter my subscription, starting from: .....

☐ I enclose a cheque for £/$ .....
(Payable to BMJ)

☐ Charge my credit card £/$.....

☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐

American Express/Visa/Mastercard/Delta/Switch
(delete as appropriate)

Switch Issue Number .....

Expiry date .....Signature .....
(Your signature is essential when paying by credit card)
If your billing address differs from below, please advise us

Name.....

Address.....

.....

Postcode .....Country .....

N.B. Subscribers in the following countries must add tax to the quoted sterling price unless they can provide a registration number: Canada - 7% GST, Italy and Spain - 4% IVA, Ireland - 21%, Germany - 7% MWS, Belgium - 6% TVA/BTW and France - 20.6% TVA

Send orders to: **BMJ Publishing Group, Journals Marketing Dept., PO Box 299, London WC1H 9TD, UK.**

Orders in the U.S: **BMJ Publishing Group, Box 509A, Kennebunkport, ME 04046, USA.**
Tel: 1-800-2-FON-BMJ Fax: 1-800-2-FAX-BMJ

INVITATION TO DELEGATES

SWEDISH HEALTH SERVICE QUALITY AWARD 1999

A Three Day Conference
Tuesday 25 - Thursday 27 May 1999
STOCKHOLM INTERNATIONAL FAIRS
SWEDEN

4th European Forum on Quality Improvement in Health Care and 4th Swedish QUL Conference

THEMES OF THE FORUM

- *Accelerating clinical improvement*
- *Quality improvement in primary care*
- *Making health better in the community*
- *Promoting evidence - based health care*
- *Building partnerships with patients*
- *Measurement for quality improvement in health care*
- *Leading change*
- *Increasing access and reducing delay in health care*
- *Harnessing information and communication technology for health improvement*
- *Putting quality improvement at the heart of education of health care professionals*

AIMS OF THE FORUM

- *To provide education on how to improve health care*
- *To exchange sound, practical ideas on improving health care*
- *To provide a setting for deep discussion and shared learning among those charged with leading improvements in health care*
- *To build the scientific base of methods to improve health care*

Book your place by 31 January 1999 and save £50 on the full registration fee

PRINCIPLES OF THE FORUM

- *Emphasis on what works*
- *Learning through experience*
- *Concentrating on improvement rather than inspection*
- *Patient orientation*
- *Multidisciplinary*
- *Basing change on measurement*
- *Team orientation*
- *Cost consciousness*
- *Encouraging efficiency*
- *All teach, all learn*

FOR FURTHER INFORMATION, PLEASE COMPLETE AND RETURN THE FORM BELOW.

INSTITUTE FOR HEALTHCARE IMPROVEMENT

Supported by

THE FEDERATION OF SWEDISH COUNTY COUNCILS

BMJ Publishing Group

Please send me further details on the 4th European Forum on Quality Improvement in Health Care and 4th Swedish QUL Conference.

Name: _____

Address: _____

_____

_____

Postcode: _____ Country: _____

Job/Position: _____

Telephone: _____ Fax: _____

E-mail: _____

Please return this form to Marchella Mitchell, BMA/BMJ Conference Unit, PO Box 295, London, WC1H 9TE.
Fax: +44 (0) 171 383 6869 Email: MMitchell@bma.org.uk

For reprints opportunities, please contact:

Sheila Williams (Quotations)
Tel: +44 (0)171 383 6305 Fax: +44 (0)171 383 6699
Email: swilliams@bmjgroup.com

Sheila Rowe (Sales Enquiries)
Tel: +44 (0)171 383 6450 Fax: +44 (0)171 383 6556
Email: jwheeler@bmjgroup.com

For enquiries within USA & Canada, please contact: Marsha Fogler
Tel: 1(800) 482 1450 or 1(609) 482 9665 Fax: 1(609) 482 7414
Email: fogler@erols.com

studentBMJ is an international monthly journal that contains similar features to the BMJ but for medical students.

studentBMJ covers subjects which matter the most to medical students everywhere.

subscriptions

To subscribe to the **studentBMJ** simply fill in the order form below. If you are a medical student in the UK you can receive the **studentBMJ** as a benefit of joining the British Medical Association (BMA).

articles & letters

Guidelines for authors are available from:
Student editor, **studentBMJ**, BMA House, Tavistock Square, London, WC1H 9JR, UK.

studentBMJ

The journal's **Education** section features articles written by experts who are asked to include the kind of information not normally found in textbooks - hints and tips that can take years of clinical experience to accumulate. Past features have included: • HIV and its Treatment • The uses of leeches in medicine • The risks of xray • Coping with surgery and loss of body parts.

The **Papers** section introduces the world of original scientific research giving medical students an insight into what lies ahead. Papers have included • Medical students attitudes towards complementary medicine • Association between alcohol and cancer

Life is where medical students write about the things that matter to them. Articles include • Heroin misuse • Community care in the South Pacific • Are you a gay medical student? • Anatomy lessons in Spain • Medical education in Brazil.

The journal's **news and student politics** section reports on issues such as • Medical student debt • Drug misuse amongst students • Medical education • New advances in medicine.

As well as this there are editorials, personal views reviews letters and much much more.

To receive a sample copy, simply complete the order form and return it to the stated address.

StudentBMJ Order Form

ISSN: 0966-6494 **Publication:** Monthly

1999 Subscription Rates These rates are valid from 1st January 1999 to 31st December 1999.

Personal Rate: £42.00 / US $68.00 **Institutional Rate:** £77.00 / US $123.00

Institutional rate applies to any library or organisation buying for the use of more than one person. US dollar rate applicable to USA subscribers only. Dollar payments must be drawn on a bank account in the USA. Sterling payments must be drawn on a bank account in the UK.

Please Tick
- ☐ Please send me a *FREE* sample copy
- ☐ Please enter my subscription starting from the month of .....
- ☐ I enclose a cheque for £/$..... *(Payable to British Medical Journal)*
- ☐ I wish to pay by credit card. £/$ .....

Personal Details (please complete in block capitals)

Name.....

Address .....

.....

Country .....Postcode.....

Email: .....

Please complete if applicable

I am studying at .....I am in year .....

Payment Details

Card Number ☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐

American Express / Visa / Mastercard / Delta / Switch *(Delete as appropriate)*

Expiry Date.....Switch issue number .....

Signature.....*(Your signature is essential, especially when paying by credit card.)*

If the credit card account holder's address differs, please advise .....

.....

.....

EC (non-UK) Customers will be charged VAT at the applicable UK rate, unless a VAT registration number is provided. Subscribers in the following areas please note: Italy and Spain must add 4% IVA, Ireland must add 21% VAT, France must add 20.6% TVA. Belgium must add 6% TVA/BTW, and Germany must add 7% MWS to the quoted sterling price. Canadian subscribers must add 7% GST.

☐ Please tick the box if you do not want your data to be used for direct marketing purposes

Please return the form to: BMJ Publishing Group, Student Subscription, PO BOX 299, London, WC1H 9TD, United Kingdom. Tel: +44(0)171 383 6270. Fax: +44(0)171 383 6402. Email: subscriptions@bmjgroup.com or BMJ Publishing Group, PO BOX 590 A, Kennebunkport, ME 04046, USA. Tel: +1-800-2-FON-BMJ. Fax: +1-800-2-FAX-BMJ. Email: bjpaige@cybertours.co

Visit the studentBMJ at: www.studentbmj.com

BMJ Publishing Group

OFFICIAL JOURNAL OF

ARIZONA MEDICAL ASSOCIATION · CALIFORNIA MEDICAL ASSOCIATION · DENVER MEDICAL SOCIETY · IDAHO MEDICAL ASSOCIATION · NEVADA STATE MEDICAL ASSOCIATION · NEW MEXICO MEDICAL SOCIETY · UTAH MEDICAL ASSOCIATION · WASHINGTON STATE MEDICAL ASSOCIATION · WYOMING MEDICAL SOCIETY

DISPLAY SHELVES

The Western Journal of Medicine

VOLUME 170 • NUMBER 2 FEBRUARY 1999

EDITORIAL

73 Children, Youth, and Families: Building on the Cultural Strengths of Hispanic and Latino Communities
J ACEVES

ARTICLES

75 Elevated Asthma Morbidity In Puerto Rican Children: A Review of Possible Risk and Prognostic Factors
M LARA, H MORGENSTERN, N DUAN, and RH BROOK

85 Latino Children's Health and the Family–Community Health Promotion Model
FS MENDOZA and E FUENTES-AFFLICK

93 Placebo Medication Use in Patient Care: A Survey of Medical Interns
JT BERGER

97 International Travel and Vaccinations
MK RIZVON, S QAZI, and LA WARD

104 Amebic Liver Abscess: Epidemiology, Clinical Features, and Outcome
RK SEETO and DC ROCKEY

ALERTS, NOTICES, AND CASE REPORTS

110 *Yersinia pseudotuberculosis* Bacteremia and Splenic Abscess in a Patient With Non–Insulin-Dependent Diabetes Mellitus
WK RATHMELL, P ARGUIN, S CHAN, and A YU

112 High-Dose Praziquantel With Cimetidine for Refractory Neurocysticercosis: A Case Report With Clinical and MRI Follow-Up
T YEE, JA BARAKOS, and RT KNIGHT

115 Diabetic Ketoacidosis in Pregnancy With a Recent Normal Screening Test
MJ O'SHAUGHNESSY, KR BEINGESSER, and WU KHIEU

118 Parathyroid Cyst: An Uncommon Cause of a Palpable Neck Mass and Hypercalcemia
SP PINNEY and PA DALY

LESSONS FROM THE PRACTICE

121 Phillip
GS REITER

OTHER FEATURES

68 Continuing Medical Education Activities
124 In Memoriam
125 Poetry
126 Classified Advertising

Detailed Table of Contents: 66,67

THE FRANCIS A. COUNTWAY LIBRARY OF MEDICINE BOSTON, MA

FEB 23 1999

Affiliated Clinical Investigation Societies: the Western Association of Physicians; the Western Society for Clinical Investigation; the Western Section, American Federation for Medical Research; the Western Society for Pediatric Research; the Western Region, Society for Investigative Dermatology

Full text, free access.

– Fully searchable archive –

– 150 topic collections –

– Customised email alerting –

– Rapid responses –

– Enhanced articles –

– Extra news stories –

– Direct Medline access –

– Jobs, courses, and careers –

And we don't ask you to pay, subscribe, register, provide passwords, or fill in interminable online questionnaires.

www.bmj.com

THE FRANCIS A. COUNTWAY LIBRARY OF MEDICINE BOSTON, MA

The Western Journal of Medicine®

SINCE 1902

P.O. BOX 7690 • SAN FRANCISCO, CALIFORNIA 94120-7690
221 MAIN STREET • SAN FRANCISCO, CALIFORNIA 94105
TELEPHONE (415) 882-5177; FACSIMILE (415) 882-3379; E.MAIL wjmsf@pacbell.net

FEB 23 1999

MICHAEL S. WILKES, *Editor*
MIRIAM SHUCHMAN, *Editor*

CATHERINE NANCARROW, *Editorial Manager*
NEIL POPPMACHER, *Production Manager*
RUTH STAUNTON, *Business Manager*

editorial communications to CATHERINE NANCARROW • business communications to RUTH STAUNTON

Official Journal of the Alaska State Medical Association, the Arizona Medical Association, the California Medical Association, the Denver Medical Society, the Idaho Medical Association, the Nevada State Medical Association, the New Mexico Medical Society, the Utah Medical Association, the Washington State Medical Association, and the Wyoming Medical Society.

Affiliated Clinical Investigation Societies: the Western Association of Physicians; the Western Society for Clinical Investigation; the Western Section, American Federation for Medical Research; the Western Society for Pediatric Research; the Western Region, Society for Investigative Dermatology.

SPECIAL EDITORS

Special Editor for Arizona
Marshall B. Block, Phoenix, Ariz

Special Editor for Denver
David Shander, Denver, Colo

Special Editor for Idaho
E. R. W. Fox, Coeur d'Alene, Idaho

Special Editor for Nevada
Anton P. Sohn, Reno, Nev

Special Editor for New Mexico
I. Brian Taylor, Carlsbad, NM

Special Editor for Utah
C. Basil Williams, Salt Lake City, Utah

Special Editor for Washington
David Hopkins, Federal Way, Wash

Special Editor for Wyoming
Joseph P. Murphy, Casper, Wyo

ASSISTANT EDITORS

Clinical Investigation
H. Benfer Kaltreider

Health and Public Policy
Ralph Crawshaw

International Health
Anvar Velji

Lessons From the Practice
Stephen J. McPhee
Jonathan E. Rodnick

Medical Staff Conferences
Nathan M. Bass

Poetry
Margaret Kaufman

Primary Care Medicine
Stephen J. McPhee
Terrie Mendelson

Radiologic Cases
Jonathan M. Levy

EDITORIAL BOARD

Editor Emeritus
Malcolm S. M. Watts, San Francisco, Calif

Anesthesiology
Carol Lake, Sacramento, Calif

Biostatistics and Epidemiology
Virginia L. Ernster, San Francisco, Calif

Cardiac and Thoracic Surgery
Norman E. Shumway, Stanford, Calif

Dermatology
Clifton R. White Jr, Portland, Ore

Emergency Medicine
William A. Boehm, Alamogordo, NM

General and Family Practice
Norman Kahn, Kansas City, Mo
Thomas E. Norris, Seattle, Wash
Joe Schoeber, Casper, Wyo

Internal Medicine
Albert Deisseroth, Houston, Texas
Alan Fogleman, Los Angeles, Calif
Patricia Gabow, Denver, Colo
John H. Holbrook, Salt Lake City, Utah
Philip Hopewell, San Francisco, Calif
Irwin J. Schatz, Honolulu, Hawaii
Walter E. Stamm, Seattle, Wash
Reginald Strickland, Albuquerque, NM
Stephen I. Wasserman, San Diego, Calif

Neurology
Robert Collins, Los Angeles, Calif
John Greenlee, Salt Lake City, Utah
Leslie Wiener, Los Angeles, Calif
Earl Zimmerman, Portland, Ore

Neurosurgery
George A. Ojemann, Seattle, Wash
Robert F. Spetzler, Phoenix, Ariz

Nuclear Medicine
Jerold M. Lowenstein, San Francisco, Calif

Obstetrics and Gynecology
Daniel Mishell Jr, Los Angeles, Calif

Occupational Medicine
Linda Rosenstock, Washington, DC

Ophthalmology
Sandy Feldman, La Jolla, Calif

Orthopedics
Thomas DeCoster, Albuquerque, NM

Pathology
Ronald Weinstein, Tuczon, Ariz

Pediatrics
Allen W. Mathies Jr, Pasadena, Calif
Diane Wara, San Francisco, Calif

Pharmacology
Rubin Bressler, Tucson, Ariz

Physical Medicine and Rehabilitation
Julie G. Madorsky, Pomona, Calif

Preventive Medicine and Public Health
Joseph L. Lyon, Salt Lake City, Utah

Psychiatry
J. Christian Gillin, San Diego, Calif
Lewis Judd, La Jolla, Calif

Radiology
Gary Glazer, Stanford, Calif
Michael L. Manco-Johnson, Denver, Colo
Albert A. Moss, Seattle, Wash

Surgery
Haile T. Debas, San Francisco, Calif
Alex G. Little, Las Vegas, Nev

Urology
Linda Shortliffe, Stanford, Calif

Senior Members at Large
Thomas Elmendorf, Davis, Calif
Edgar Wayburn, San Francisco, Calif

ADVISORY BOARD, CLINICAL INVESTIGATION

Brian A. Cason, San Francisco, Calif
John Christenson, Salt Lake City, Utah
Kari Connolly, San Francisco, Calif
Bruce W. Goldberg, Portland, Ore
Philip Goodman, Reno, Nev
Roy Jones, Albuquerque, NM
Howard Lien, Tucson, Ariz
Barbara M. Lippe, Los Angeles, Calif
Michael W. McDermott, San Francisco, Calif
Jeanette Mladenovic, Denver, Colo
Kenneth M. Moser, San Diego, Calif
James C. Orcutt, Seattle, Wash
John Owings, Sacramento, Calif
Robert Robbins, Stanford, Calif
Henry Rosen, Seattle, Wash
Mary H. Samuels, Portland, Ore
George A. Sarosi, San Jose, Calif
Jeffrey Saver, Los Angeles, Calif
David Schriger, Los Angeles, Calif
Jack H. Simon, Denver, Colo
Peggy Sue Weintrub, San Francisco, Calif
Owen M. Wolkowitz, San Francisco, Calif

DISPLAY ADVERTISING INFORMATION

CONTACT: Alan Walker, BMJ Publishing Group, BMA House, Tavistock Square, London WC1H 9JR, UK • (+44) 171-383-6226/FAX (+44) 171-383-6556. Email: awalker@bmj.com

Advertisements—The journal is published the second week of the month. Display advertising must be received no later than the first of the month preceding issue. Advertising rates will be sent on request. Acceptance of advertising is contingent upon approval by the Publisher.

The journal reserves the right to reject any advertisement.

CLASSIFIED ADVERTISING

CONTACT: Ruth Staunton, The Western Journal of Medicine, P.O. Box 7690, San Francisco, CA 94120-7690 • (415) 882-5177/FAX (415) 882-3379.

SUBSCRIPTION INFORMATION

The subscription price is $70 per year and $130 for 2 years in the United States and Canada (US funds); $85/$160 in all other countries. Institutional rate in the United States is $120/$240; $130/$260 all other countries. Single copies are $15. Address all subscription communications to:

THE WESTERN JOURNAL OF MEDICINE, P.O. Box 7690, San Francisco, CA 94120-7690 • Tel: (415) 882-5177

Allow six weeks for subscriptions to begin. Past issues must be bought individually. So long as reserve stocks are available, missing issue requests from subscribers are honored for up to six months after the issue date. Thereafter, the single copy rate of $15 is applicable for each issue available.

Change of Address—Requests for change of address should give both the old and new address. Allow six weeks for changeover.

SUBMITTING MANUSCRIPTS

Manuscripts for consideration should be sent to the editorial manager, C. Nancarrow, The Western Journal of Medicine, P.O. Box 7690, San Francisco, CA 94120-7690.

"Instructions for Authors"—A complete guide to manuscript submission and *WJM* style available from the publisher. Manuscripts may be prepared in accordance with the "Uniform Requirements for Manuscripts Submitted to Biomedical Journals."

PUBLISHER

Copyright © 1999 by the British Medical Journal Publishing Group • Owned and Published by BMJ Publishing Group and UCSF Stanford Healthcare

All material subject to this copyright appearing in THE WESTERN JOURNAL OF MEDICINE may be photocopied for the noncommercial purpose of scientific or educational advancement. Volumes begin with January and July.

THE WESTERN JOURNAL OF MEDICINE (ISSN 0093-0415/USPS 084 480) is published monthly by BMJ Publishing Inc, 221 Main St., San Francisco, CA 94105. (Mail correspondence to BMJ Publishing Inc., P.O. Box 7690, San Francisco, CA 94120-7690. Periodicals postage paid at Easton, Pennsylvania.

POSTMASTER: Send address changes to *The Western Journal of Medicine*, P.O. Box 7690, San Francisco, CA 94120-7690.

The Western Journal of Medicine

VOLUME 170 • NUMBER 2 • FEBRUARY 1999

CONTENTS

EDITORIAL

73 **Children, Youth, and Families: Building on the Cultural Strengths of Hispanic and Latino Communities**

JAVIER ACEVES, MD

Clinical Associate Professor of Pediatrics, University of New Mexico, Albuquerque, New Mexico

ARTICLES

75 **Elevated Asthma Morbidity In Puerto Rican Children: A Review of Possible Risk and Prognostic Factors**

MARIELENA LARA, MD, MPH; HAL MORGENSTERN, PHD; NAIHUA DUAN, PHD; and ROBERT H. BROOK, MD, SCD

From the UCLA/RAND Program on Latino Children with Asthma, Division of General Pediatrics, UCLA Department of Pediatrics, Los Angeles, California, RAND Health, Santa Monica, California; and the Center for Occupational and Environmental Health, Department of Epidemiology, UCLA School of Public Health, Los Angeles, California.

85 **Latino Children's Health and the Family–Community Health Promotion Model**

FERNANDO S. MENDOZA, MD, MPH, and ELENA FUENTES-AFFLICK, MD, MPH

From the Department of Pediatrics, Stanford University School of Medicine, Palo Alto, California; and the Department of Pediatrics, University of California, San Francisco, California.

93 **Placebo Medication Use in Patient Care: A Survey of Medical Interns**

JEFFREY T. BERGER, MD, FACP

From the Department of Medicine, Winthrop-University Hospital, Mineola, New York.

97 **International Travel and Vaccinations**

MOHAMMED KALEEM RIZVON, MBBS; SAMIA QAZI, MBBS; and LAURIE ANNE WARD, MD

From the Division of General Internal Medicine, Nassau County Medical Center, East Meadow, New York.

104 **Amebic Liver Abscess: Epidemiology, Clinical Features, and Outcome**

REGINALD K. SEETO, MB, BS; and DON C. ROCKEY, MD

From the Departments of Medicine/Divisions of Gastroenterology, University of California, San Francisco, California; and Duke University Medical Center, Durham, North Carolina.

ALERTS, NOTICES, AND CASE REPORTS

110 ***Yersinia pseudotuberculosis* Bacteremia and Splenic Abscess in a Patient With Non–Insulin-Dependent Diabetes Mellitus**

W. KIMRYN RATHMELL, MD, PHD; PAUL ARGUIN, MD; STEPHANIE CHAN, MD; and ALBERT YU, MD

From the Department of Medicine and the Division of Infectious Diseases, Stanford University School of Medicine, Stanford, California; and the Department of Medicine, Santa Clara Valley Medical Center, San Jose, California.

112 **High-Dose Praziquantel With Cimetidine for Refractory Neurocysticercosis: A Case Report With Clinical and MRI Follow-Up**

THOMAS YEE, DO; JEROME A. BARAKOS, MD; and ROBERT T. KNIGHT, MD

From the VA Palo Alto Health Care System, Palo Alto, California, and the Department of Neurology and Neurological Sciences, Stanford University, School of Medicine, Stanford, California; the Department of Radiology, California Pacific Medical Center and the University of California, San Francisco, California; and the VA Northern California Health Care System, Martinez, California, and the Department of Neurology, University of California-Davis, Davis, California.

115 **Diabetic Ketoacidosis in Pregnancy With a Recent Normal Screening Test**

MICHAEL J. O'SHAUGHNESSY, MD; KELLI R. BEINGESSER, MD; and WILLIAM U. KHIEU, MD

From the University Medical Center, University of California, San Francisco Fresno-Central San Joaquin Valley Medical Education Program, Fresno, California.

118 **Parathyroid Cyst: An Uncommon Cause of a Palpable Neck Mass and Hypercalcemia**

SEAN P. PINNEY, MD; and PATRICIA A. DALY, MD

From the Department of Internal Medicine, Beth Israel Deaconess Medical Center - West Campus, and the Division of Endocrinology and Metabolism, Beth Israel Deaconess Medical Center, Boston, Massachusetts.

LESSONS FROM THE PRACTICE

121 **Phillip**

GARY S. REITER, MD, FACP

From the University of Massachusetts, Holyoke, Massachusetts.

OTHER FEATURES

68 **Continuing Medical Education Activities**

124 **In Memoriam**

125 **Poetry**

126 **Classified Advertising**

★ Official Journal of the Alaska State Medical Association, the Arizona Medical Association, the California Medical Association, the Denver Medical Society, the Idaho Medical Association, the Nevada State Medical Association, the New Mexico Medical Society, the Utah Medical Association, the Washington State Medical Association, and the Wyoming Medical Society.

Continuing Medical Education

ARIZONA • CALIFORNIA, HAWAII, NEVADA • COLORADO • IDAHO • NEW MEXICO • UTAH • WASHINGTON • WYOMING

ARIZONA

The following list of continuing medical education programs in Arizona is compiled by the Arizona Medical Association. All courses listed have been certified as meeting the criteria for Category I of the ArMA CME Certificate and the AMA Physicians Recognition Award. To list Category I continuing medical education programs, please send information to Arizona Medical Association, 810 West Bethany Home Road, Phoenix, AZ 85013; or phone (602) 246-8901.

Brochures and registration forms are available from the contact person or organization sponsoring the program.

February 26–28, 1999—**Coronary Heart Disease Update.** Hilton Tapatio Cliffs, Phoenix, AZ. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569 (800)421-3756 FAX (303)798-5731.

October 29–31, 1999—**Neurology for the Non-neurologist.** The Phoenician, Scottsdale, AZ. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569 (800)421-3756 FAX (303)798-5731.

December 10–12, 1999—**Managing Respiratory Disease.** The Phoenician, Scottsdale, AZ. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569 (800)421-3756 FAX (303)798-5731.

CONTACT INFORMATION

ArMA—Contact: Arizona Medical Association, 810 W Bethany Home Rd, Phoenix, AZ 85013. (602) 246-8901.

Mayo Clinic-Scottsdale—Contact: Postgraduate Courses, Mayo Clinic-Scottsdale, (602) 301-7447.

U of A—Contact: University of Arizona College of Medicine, Arizona Health Sciences Center, Tucson, AZ 85724. (520) 626-7832; (800) 328-5868.

CALIFORNIA, HAWAII, AND NEVADA

This listing of continuing education programs in California, Hawaii, and Nevada is supplied by the Committee on Continuing Medical Education of the California Medical Association. All courses and meetings listed have been approved for Category I credit toward the CMA Certificate in Continuing Medical Education. To have accredited courses listed here, please send information at least two months in advance to Paulette Richardson, Continuing Medical Education, California Medical Association, PO Box 7690, San Francisco 94120-7690; or phone (415) 882-3387. For more information on accreditation or certification, please write to the above address.

ALLERGY/IMMUNIZATION

August 13–15—**A Midsummer Night's Wheeze.** California Society of Allergy, Asthma and Immunology at La Costa Resort and Spa, Carlsbad, CA. Fri–Sun 12 hrs. $145-$199. Contact: CSAAI Conference Management at (714) 828-8022.

ANESTHESIOLOGY

November 5–7, 1999—**11th Annual Anesthesiology Update.** Monterey Plaza, Monterey, California. Fri–Sat. Contact (916) 734-5390.

CARDIOLOGY

February 18–20, 1999—**19th Annual Pathophysiology & Techniques of Cardiopulmonary Bypass.** San Diego Marriott Hotel & Marina. Sponsored by the Cardiothoracic Research &Education Forum. Contact: Aligned Management Associates, Inc. P.O. Box 23220, San Diego CA 92193 (619) 541-1444 or fax (619) 541-1447. www.amainc.com

March 24–26, 1999—**Coronary Heart Disease Update.** Maui, HI; July 30–August 1, 1999–Yosemite, CA; November 19–21, 1999–Las Vegas, NV. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569 (800)421-3756 FAX (303)798-5731.

April 17, 1999—**Primary Care Cardiology.** UC Davis at Cancer Center Auditorium, Sacramento, CA. Sat. Contact: UCD (916) 734-5390.

DERMATOLOGY

March 4–7, 1999—**Practical Dermatology for the Primary Care Physician, Orlando, FL.** Sponsored by Continuing Medical Education Associates. To be held at the Buena Vista Palace at Walt Disney World Village, Orlando, FL. Method: AV, L, SB, W. Thus–Sun. 20 hrs credit: AMA, AOA, AAFP. $575. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

May 23–26, 1999—**Practical Dermatology for the Primary Care Physician, Las Vegas, NV.** Sponsored by Continuing Medical Education Associates. To be held at the Caesars Palace, Las Vegas, NV. Method: AV, L, SB, W. Sun–Wed. 20 hrs credit: AMA, AOA, AAFP. $575. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

March 12–14, 1999—**Dermatology for the Non-Dermatologist.** Las Vegas, NV; April 23–25, 1999–San Francisco, CA; June 25–27, 1999–Anaheim, CA; September 24–26, 1999–Las Vegas, NV. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569 (800)421-3756 FAX (303)798-5731.

EMERGENCY MEDICINE

March 1–2, 1999—**Improving Emergency Department Patient Satisfaction and Reducing Length of Stay.** Las Vegas, Nevada at Harrah's. Contact: CEME, 5330 Primrose Drive, Suite 250, Fair Oaks, CA 95628. (800) 651-2363.

March 1–5, 1999—**Critical Care, Trauma and Emergency Medicine, 37th Annual Symposium.** Sponsored by the University of Southern California School of Medicine, Postgraduate Division. Caesars Palace Hotel, Las Vegas, NV. 27 hrs. Contact Associate Dean, USC Postgraduate Medicine, 1975 Zonal Ave., KAM 307, Los Angeles, CA 90033. (323) 442-2555 or (800) USC-1119 or FAX (323) 442-2152.

April 12–13, 1999—**High Risk Emergency Medicine.** Las Vegas, Nevada at Harrah's. Contact: CEME, 5330 Primrose Drive, Suite 250, Fair Oaks, CA 95628. (800) 651-2363.

May 6–7, 1999—**Challenges in Pediatric Emergency Medicine.** Las Vegas, Nevada at Harrah's. Contact: CEME, 5330 Primrose Drive, Suite 250, Fair Oaks, CA 95628. (800) 651-2363.

May 13–16, 1999—**Outdoor Emergency Medicine, Scottsdale, AZ.** Sponsored by Continuing Medical Education Associates. To be held at the Marriott Camelback Inn, Scottsdale, AZ. Method: AV, L, SB, W. Thurs–Sun. 32 hrs credit: AMA, AOA, AAFP. $750. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

May 20–21, 1999—**High Risk Emergency Medicine.** Las Vegas, Nevada at Harrah's. Contact: CEME, 5330 Primrose Drive, Suite 250, Fair Oaks, CA 95628. (800) 651-2363.

June 3–4, 1999—**Improving Emergency Department Patient Satisfaction and Reducing Length of Stay.** Chicago, IL at the Holiday Inn Chicago City Centre. Contact: CEME, 5330 Primrose Drive, Suite 250, Fair Oaks, CA 95628. (800) 651-2363.

August 16–19—**National Emergency Medicine Board Review.** American College of Emergency Physicians at Harrah's Las Vegas, NV. Mon–Thurs. 40 hrs. $395. Contact: Center for Emergency Medical Education (800) 651-CEME (2363).

ENDOCRINOLOGY

March 5, 1999—**Diabetes Update: 1999.** UC Davis at Doubletree Hotel, Sacramento, CA. Friday. 7 hrs. $130. Contact: UCD (916) 734-5390.

March 11–13, 1999—**The Fourth International Conference on Continuous Renal Replacement Therapies.** Hotel del Coronado in San Diego, California. Contact: Shirley Kolkey, Complete Conference Management, 1660 Hotel Circle North, #220, San Diego, CA 92108. (619) 299-6673 or fax (619) 299-6675.

October 22–24, 1999—**Clinical Endocrinology for Primary Care Physicians.** Tropicana, Las Vegas, NV. CME 11 hrs Category 1. Contact: Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569 (800)421-3756 FAX (303)798-5731.

ETHICS

March 3, 1999— **Ethical Problems of Daily Practice.** UC Davis at Cancer Center Auditorium, Sacramento. Wed. 6.5 hrs. Contact: UCD (916) 734-5390.

FAMILY PRACTICE/PRIMARY CARE

February 17–19, 1999—**Annual Review in Family Medicine: Controversies and Challenges in Primary Care.** UCSF at Cathedral Hill Hotel, SF. Wed.–Fri. 16 hrs. $400. Contact: UCSF Program Coordinator, Dept. of Family and Community Medicine (415) 476-5250.

March 27, 1999—**Primary Care Gastroenterology.** UC Davis at Cancer Center Auditorium, Sacramento, CA. Saturday. Contact: UCD (916) 734-5390.

April 28, 1999—**Mangement of Benign Uterine Conditions.** UC Davis at Cancer Center Auditorium, Sacramento, CA. Wed. 4 hrs. $50. Contact: UCD (916) 734-5390.

May 14–18, 1999—**Primary Care Essentials, San Francisco,** CA. Sponsored by Continuing Medical Education Associates. To be held at the Grand Hyatt on Union Square, San Francisco, CA. Method: AV, L, SB, W. Thurs–Sun. 32 hrs credit: AMA, AOA, AAFP. $750. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

May 23–26—**Office Orthopedics and Bone Radiology for the Primary Care Physician.** CMEA at Caesar's Palace, Las Vegas, NV. Sun–Wed, 20 hrs, $575. Contact: Victoria Gonzalez, P.O. Box 270469, San Diego, CA 92198; (800) 993-2632 or (619) 674-5200.

May 23–26—**Practical Dermatology for the Primary Care Physician.** CMEA at Caesar's Palace, Las Vegas, NV Sun–Wed. 20 hrs. $575. Contact: Victoria Gonzalez, P.O. Box 270469, San Diego, CA 92198; (800) 993-2632 or (619) 674-5200.

June 5–7—**8th Annual Primary Care Treatment of Pain.** UC Davis at Tenaya Lodge at Yosemite Fish Camp, CA. Sat–Mon. Contact: UCD (916) 734-5390

June 13–18—**23rd Annual Fingers to the Toes Primary Care Orthopaedics.** UC Davis at Stanford Sierra Camp, near South Lake Tahoe. Sun–Fri. Contact: UCD (916) 734-5390

July 5–8—**Family Practice Board Review Course.** UCSF at Fairmont Hotel, SF. Mon–Thurs. 25 hrs. $525–$575. Contact: Program Coordinator, Dept. Family and Community Medicine, 500 Parnassus Ave, MU-3E, SF, CA 94143-0900 or phone (415) 476-5250.

July 25–29—**19th Annual Current Concepts in Primary Care Cardiology.** UC Davis at Granlibakken Conference Center, Tahoe City, CA. Sun–Thurs. Contact: UCD (916) 734-5390.

KEY TO ABBREVIATIONS

DREW:	Charles R. Drew Postgraduate Medical School, Office of Continuing Medical Education, (213) 563-4800.
LLU:	Loma Linda University, Continuing Medical Education Programs, (909) 824-4963.
STAN:	Stanford University, Postgraduate Education, (415) 723-5594.
UCD:	University of California, Davis, Office of Continuing Medical Education, (916) 734-5390.
UCI:	University of California, Irvine, Memorial/UCI Center for Health Education, (714) 824-5926.
UCLA:	University of California, Los Angeles, Continuing Education in Medicine and Health Sciences, (310) 794-2620.
UCSD:	University of California, San Diego, Office of Continuing Medical Education, (619) 534-3940.
UCSF:	University of California, San Francisco, Extended Programs in Medical Education, (415) 476-4251.
USC:	University of Southern California, Postgraduate Division, (800) USC-1119.

INFECTIOUS DISEASE

February 21–26, 1999—**Winter Course in Infectious Diseases, Snowmass, Colorado-25th Anniversary Meeting.** Sponsored by the Division of Infectious Diseases and Geographic Medicine, Stanford University School of Medicine and Research Institute, Palo Alto Medical Foundation. 28 hrs. $75–$350. Contact: Trisha Mitchell, Meeting Coordinator (800) 535-7814 or fax (215) 422-1283.

March 12, 12:30–2:00 p.m.—**Early Adolescents: How to Save Their Lives.** California Department of Health Services at Distance Learning Facilities. Thurs. 2.5 hrs. Free. Contact: CDLHN (619) 594-3652.

INTERNAL MEDICINE

March 19–25, 1999—**Internal Medicine, San Diego** CA. Sponsored by Continuing Medical Education Associates. To be held at the Hotel del Coronado, San Diego, CA. Method: AV, L, SB, W. Fri–Thurs. 45 hrs credit: AMA, AOA, AAFP. $895. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

August 22–27, 1999—**New Advances in Internal Medicine.** UC Davis at Embassy Suites, Monterey, CA. Sun–Fri. Contact UCD (916) 734-5390.

NEUROLOGY

May 14–16, 1999—**Neurology for the Non-neurologist.** Bally's, Las Vegas, NV. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569 (800)421-3756 FAX (303)798-5731.

OB/GYN

February 25–28, 1999—**Office Gynecology and Women's Health for the Primary Care Physician, Orlando, FL.** Sponsored by Continuing Medical Education Associates. To be held at the Buena Vista Palace at Walt Disney World Village, Orlando, FL. Method: AV, L, SB, W. Thurs–Sun. 20 hrs credit: AMA, AOA, AAFP. $575. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

February 27–March 2, 1999—**16th Annual OB/GYN Conference.** OCD at Harrahs Tahoe, South Lake Tahoe, NV. Sat.–Tues. 16 hrs. $325. Contact: UCD (916) 734-5390.

April 28, 1999—**Mangement of Benign Uterine Conditions.** UC Davis at Cancer Center Auditorium, Sacramento, CA. Wed. 4 hrs. $50. Contact: UCD (916) 734-5390.

September 25–26, 1999—**Ultrasound Update: 1999.** Hilton Hotel, Sacramento, CA. Sat.–Sun. (916) 734-5390.

December 10–12,1999—**Issues in Women's Health.** Tropicana, Las Vegas, NV. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569 (800)421-3756 FAX (303)798-5731.

OCCUPATIONAL & ENVIRONMENTAL

May 14–15—**Occupational and Environmental Medicine: 1999.** UC Davis at Cancer Center Auditorium, Sacramento. Fri–Sat. Contact: UCD at (916) 734-5390.

OPHTHALMOLOGY

May 21—UC **Davis Annual Ophthalmology Symposium.** UC Davis at the Hilton Hotel, Sacramento. Fri. Contact: UCD (916) 734-5390.

ORTHOPEDICS

February 25–28, 1999—**Office Orthopedics and Bone Radiology for the Primary Care Physician, New Orleans, LA.** Sponsored by Continuing Medical Education Associates. To be held at the Royal Sonesta Hotel, New Orleans, LA. Method: AV, L, SB, W. Thurs–Sun. 20 hrs credit: AMA, AOA, AAFP. $575. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

February 25–28, 1999—**Office Orthopedics and Bone Radiology for the Primary Care Physician, Las Vegas, NV.** Sponsored by Continuing Medical Education Associates. To be held at the Caesars Palace, Las Vegas, NV. Method: AV, L, SB, W. Sun–Wed. 20 hrs credit: AMA, AOA, AAFP. $575. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

April 10, 1999—**Primary Care Orthopedics, Lower Extremities.** UC Davis at Holiday Inn Northeast, Sacramento, CA. Sat. Contact: UCD (916) 734-5390.

June 13–18, 1999—**23rd Annual Fingers to the Toes Primary Care Orthopaedics.** To be held at the Stanford Sierra Camp, near South Lake Tahoe, Fallen Leaf Lake, CA. Sun–Fri. Contact (916) 734-5390.

PEDIATRICS

February 14–17, 1999—**Pediatrics Update 1999, San Diego, CA.** Sponsored by Continuing Medical Education Associates. To be held at the Hyatt Islandia, San Diego, CA. Method: AV, L, SB, W. Sun–Wed. 20 hrs credit:AMA, AOA, AAFP. $575. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

February 20—**Dintinguished Psychiatrists Symposium: A Special Update for Clinicians on New Treatment Advances for Depression.** UC Davis at UC Davis Cancer Center Auditorium, Sacramento. Sat. 3.5 hrs. $55. Contact: UCD (916) 734-5390.

February 28–March 3, 1999—**Pediatrics Update 1999, Orlando, FL.** Sponsored by Continuing Medical Education Associates. To be held at the Buena Vista Palace at Walt Disney World Village, Orlando, FL. Method: AV, L, SB, W. Sun–Wed. 20 hrs credit:AMA, AOA, AAFP. $575. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

March 19–20, 1999—**Pediatrics Update: 1999.** UC Davis at Cancer Center Auditorium, Sacramento, CA. Fri–Sat. Contact: UCD (916) 734-5390.

May 6–8, 1999—**Advances and Controversies in Clinical Pediatrics.** UCSF at Ritz-Carlton Hotel on Nob Hill, SF. Contact: UCSF (415) 476-5808 or FAX (415) 502-1795.

May 17–19—**18th Annual Conference on Child Abuse and Neglect.** UC Davis at the Radisson Hotel, Sacramento. Mon–Wed. 21 hrs. $195. Contact: UCD at (916) 734-5390.

July 16–17,1999—**Seventh Annual Pediatric Update.** Sponsored by Lucile Packard Children's Health Services at Stanford and faculty from UCSF and Stanford Schools of Medicine. Lucile Packard Children's Hospital. Contact: Elinor Meyer, Continuing Medical Education and Physician Relations Department, Lucile Packard Children's Hospital, 725 Welch Road, Palo Alto,CA 94304 (650) 497-8554.

PLASTIC SURGERY

March 18–20, 1999—**11th Annual Symposium on Aesthetic Surgery.** UCSF at Palace Hotel, San Francisco. Thurs–Sat. 19.5 hrs. $950. Contact UCSF (415) 476-5808.

PRIMARY CARE

February 26–28, 1999—**Management of the HIV-Infected Patient–A Practical Approach for the Primary Care Practitioner.** Le Meridien, New Orleans, LA. Contact: Center for Bio-Medical Communication, Inc. (201) 342-5300 or FAX (201) 342-7555; email cmeinfo@cbcbiomed.com

March 27, 1999—**Primary Care Gastroenterology.** UCDMC, Cancer Center Auditorium, Sacramento, CA. Sat. (916) 734-5390.

April 10, 1999—**Primary Care Orthopedics, Lower Extremities.** Holiday Inn Northeast, Sacramento, CA. Sat. (916) 734-5390.

April 17, 1999—**Primary Care Cardiology.** UCDMC, Cancer Center Auditorium, Sacramento, CA. Sat. (916) 734-5390.

June 5–7, 1999—**8th Annual Primary Care Treatment of Pain.** Tenaya Lodge at Yosemite, Fish Camp, CA. Sat–Mon. (916) 734-5390.

July 25–29, 1999—**19th Annual Current Concepts in Primary Care Cardiology.** Granlibakken Conference Center, Tahoe City, CA. Sun–Thurs. (916) 734-5390.

October 22–24, 1999. **Clinical Endocrinology for Primary Care Physicians.** Tropicana, Las Vegas, NV. CME 11 hrs Category 1. Contact: Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569 (800)421-3756 FAX (303)798-5731.

PSYCHIATRY

April 10, 1999—**Psychiatry Update.** UC Davis at Cancer Center Auditorium, Sacramento, CA. Sat. Contact: UCD (916) 734-5390.

RADIOLOGY

February 25–28, 1999—**Up to Date Radiology in the Desert.** Mira Monte Resort, Indian Wells, California. Credit 26 hrs. AMA. $495-$750. Contact: Ryals & Associates, Inc., PO Box 1925, Roswell, GA, 30077-1925; (770)641-9773; fax (770)552-9859; email: webmaster@ryalsmeet.com.

RESPIRATORY

March 19–20, 1999—**Cystic Fibrosis Caregivers Symposium.** UC Davis at Marriott Hotel, Napa, CA. Fri–Sat. Contact: UCD (916) 734-5390.

Managing Respiratory Disease–April 23–25, 1999–Las Vegas, NV; June 11–13, 1999–San Francisco, CA; August 6–8, 1999–Monterey, CA. CME 11 hrs Category 1. Contact: Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569 (800)421-3756 FAX (303)798-5731.

SURGERY

April 24, 1999—**3rd Annual Organ Transplant Conference.** UCD at Cancer Center Auditorium, Sacramento, CA. Sat. Contact UCD (916) 734-5390.

May 27–29—**2nd Annual Current Issues in Anatomic Pathology –1999.** UCSF at Mark Hopkins Intercontinental Hotel, SF. Thurs–Sat. 19.5 hrs. $595. Contact: UCSF (415) 476-5808.

GENERAL/MULTIDISCIPLINARY

April 23–25—**Physician Leadership Program.** California Academy of Family Physicians at Claremont Hotel, Berkeley. Fri–Sun. 20 hrs. $1245–$1395. Contact: Laura Johnson Morasch (415) 394-9121. Web: www.familydocs.org/Orgs?hcli.html E-mail: HCLI@familydocs.org.

April 28–May 8, 1999—**Blue Water Medical Seminar.** Tri City Medical Center at Baja California aboard Royal Star Sportfisher. Wed–Sun. 20 hrs. $3300. Contact: Ronald Medak (760) 727-7863.

May 16–19, 1999—**Alternative Medicine, Scottsdale, AZ.** Sponsored by Continuing Medical Education Associates. To be held at the Mariott Camelback Inn, Scottsdale, AZ. Method: AV, L, SB, W. Sun–Wed. 20 hrs credit: AMA, AOA, AAFP. $575. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

May 25 & 26—**BLS Instructor Course.** American Heart Association at San Leandro. Tues–Wed. 11 hrs. $120. Contact: CPR Seminar (925) 754-7900.

June 22–29—**Wellness in Practice: Mindfulness-Based Stress Reduction in Mind/Body Medicine.** Enloe Medical Center at Mana L'ea Retreat Center, Maui. Tues–Tues. Contact: Maui Stress Reduction Retreats, Steve (530) 898-1495.

August 24–25—**BLS Instructor Course.** American Heart Association at San Leandro. Tues–Wed. 11 hrs. Contact: CPR Seminars (925) 754-7900.

October 15–17—**Physician Leadership Program.** California Academy of Family Physicians at Laurel Heights Conference Center, SF. Fri–Sun. 20 hrs. $1245–$1395. Contact: Laura Johnson Morasch (415) 394-9121. Web: www.familydocs.org/ Orgs?hcli.html (e-mail: HCLI@familydocs.org).

LOSS PREVENTION

September 22–25, 1999—**Legal Issues in Damaged Brain Injury Cases.** Westin St. Francis Hotel, San Francisco, CA. Wed–Sat. Contact (916) 734-5390.

HOME STUDY/SELF ASSESSMENT

California Physicians' Legal Handbook Series. California Medical Association. Contact: CMA, PO Box 7690, San Francisco 94120-7690. (800) 882-1262.

Breast Cancer, Early Detection and Control. Texas Medical Association. **CD ROM.** $70. 2 hrs. Contact: Texas Medical Association, (800) 880-1300; http://www.texmed.org/health_science/hs_poep.html

COLORADO

This listing of continuing medical education programs in Colorado is compiled by the Denver Medical Society. To list CME programs here, please send information at least two months in advance to: Mr Robert L. Kennedy, Denver Medical Society, 1850 Williams Street, Denver, CO 80218; or telephone (303) 377-1850.

Brochures, course information, and registration forms are available from the contact person or organization.

Tuesday Noon Conferences—**Various Topics in Medicine.** Lutheran Medical Center, Wheat Ridge. Contact: Jean A. Kline, (303) 425-2951.

First Wednesday of Each Month—**Various Topics in Neurology.** Colorado Society of Clinical Neurologists. Contact: Colorado Society of Neurologists, (303) 449-3566.

Second Wednesday of Each Month—**Cardiovascular Education Series.** St Anthony Hospital at St Anthony Hospital, Denver. Contact: Rose Powell, (303) 629-3678.

February 19–21, 1999—**Managing Respiratory Diseases.** Marriot's Casa Marina, Key West, FL. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

February 25–27, 1999—**Dermatology For The Non-Dermatologist.** Atlantis Paradise Resort, Bahamas. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

February 26–28, 1999—**Coronary Heart Disease Update.** Hilton Tapatio Cliffs, Scottsdale, AZ. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

March 12–14, 1999—**Dermatology For The Non-Dermatologist.**Riviera Hotel & Casino, Las Vegas, NV. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

March 25–27, 1999—**Neurology For The Non-Neurologist.** Grand Beach Resort, St. Thomas, USVI. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

March 25–27, 1999—**Clinical Endocrinology For Primary Care Physicans.** Marriott's Beach Resort, St. Grand Cayman. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

March 26–28, 1999—**Managing Respiratory Diseases.** Buena Vista Palace,Orlando,FL. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

April 8–10, 1999—**Coronary Heart Disease Update.** Hyatt Regency, Aruba Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

April 8–10, 1999—**Clinical Endocrinology For Primary Care Physicans.** The Westin Resort, St John, USVI. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

April 9–11, 1999—**Arrhythmias: Interptretation, Diagnosis &Management** Hilton Tapatio Cliffs, Scottsdale, AZ. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

April 9–11, 1999—**Neurology For The Non-Neurologist.** Marriott's Casa Marina, Key West, FL. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

April 23–25,1999—**Managing Respiratory Diseases.** Bally's, Las Vegas, NV. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

April 23–25,1999—**Dermatology For The Non-Dermatologist.** Parc Fifty-five, San Francisco, CA. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

April 30–May 2, 1999—**Dermatology For The Non-Dermatologist.** South Sea Plantation, Captiva Island, FL. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

April 30–May 2, **Clinical Endocrinology For Primary Care Physicans.** Hyatt Regency, New Orleans, LA. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

May 14–16, 1999—**Managing Respiratory Diseases.** Hilton Resort, Hilton Head, SC. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

May 14–16, 1999—**Neurology For The Non-Neurologist.** Bally's, Las Vegas, NV. Fee $375. Contact Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

CONTACT INFORMATION

U of Colo—Contact: University of Colorado Health Sciences Center, School of Medicine, Office of Continuing Medical Education, 4200 E 9th Ave, Denver 80262. (303) 372-9050 or (800) 882-9153; FAX (303) 372-9065.

IDAHO

The listing of continuing medical education programs in Idaho is compiled by the Ada County Medical Society. To list CME programs here, please send information at least two months in advance to: Ada County Medical Society, Inc. 305 W. Jefferson, PO Box 2668, Boise, Idaho 83701. (208) 336-2930.

Brochures, course information, and registration forms are available from the contact person or organization.

February 19–21, 1999—**ACMS 40th Annual Medical Winter Clinics.** McCall, Idaho, Shore Lodge Inn. 11.5 hrs. Contact: Judy Barningham (208) 336-2930 or Marie Chester (208) 331-1478.

NEW MEXICO

Information, requests for accreditation, and items to be listed should be sent to the chair of the CME Committee, New Mexico Medical Society, 7770 Jefferson, Suite 400, Albuquerque, NM 87109, at least two months in advance. For information on CME accreditation or on the CME requirements of the New Mexico Board of Medical Examiners, please write to the above address or call (505) 828-0237.

NOTE: Course information in the following listing is subject to change on occasion. Check with the sponsoring institution for current details.

Every First and Third Tuesday—**Building and Implementing Clinical Practice Guidelines at the Point of Care.** Contact: Thomas A. Naegele, DO, (505) 275-7267.

April 28–30, 1999—**The Fourth Annual Clinical Cardiology Management and Diagnostic Dilemmas.** Eldorado Hotel, Santa Fe, NM. 17 Category 1 AMA. Contact: Registration Secretary, American College of Cardiology, 9111 Old Georgetown Rd, Bethesda, MD 20814-1699 (800) 253-4636, ext. 695.

July 30–August 1, 1999–**Neurology for the Non-neurologist.** Eldorado Hotel, Sante Fe, NM. CME 11 hrs Category 1. Contact: Linda Main, Meetings Coordinator, Medical Education Resources, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569 (800)421-3756 FAX (303)798-5731.

SATELLITE COURSES

Contact: Joe Treat or Jim Cato, Immunization Program, (505) 827-2366.

CONTACT INFORMATION

UNM SOM—University of New Mexico School of Medicine, Office of CME, PO Box 713, Albuquerque 87131. (505) 277-3942.

UTAH

This listing of continuing medical education courses in Utah is compiled and edited by the CME office of the Utah Medical Association. All courses listed have been certified by CME accredited institutions as meeting the criteria for Category 1 of the Physician's Recognition Award of the American Medical Association. Accredited institutions wishing to list AMA Category 1 CME courses here should send information at least two months in advance to the Office of Continuing Medical Education, 540 East Fifth South, Salt Lake City, UT 84102; or

phone (801) 355-7477. For information on CME accreditation, please write the CME office at the above address.

NOTE: Course information in the following listing is subject to change on occasion. Check with the sponsoring institution.

January 6–10, 1999—**MRI at Snowbird**. Cliff Lodge, Snowbird, Utah. Credit 20 hrs. AMA. $400-$650. Contact: Ryals & Associates, Inc., PO Box 1925, Roswell, GA, 30077-1925; (770)641-9773 or fax (770)552-9859; email: webmaster@ryalsmeet.com. www.ryalsmeet.com

MEDICAL GRAND ROUNDS

Weekly—**Grand Rounds in Internal Medicine, Psychiatry, OB/GYN, and Pediatrics.** Contact: UUSM.

Weekly—**Pediatric Grand Rounds.** Contact: PCMC.

WASHINGTON

The listing of continuing medical education programs in Washington state is compiled by the Washington State Medical Association. To list Category 1 programs here, please send information at least two months in advance to Continuing Medical Education, Washington State Medical Association, 2033 Sixth Avenue, Suite 1100, Seattle, WA 98121; or phone (206) 441-9762 or (800) 552-0612.

Brochures and registration forms are available from the contact person or organization listed at the end of each course or in the list of course sponsors and contact information.

COURSE SPONSORS AND CONTACT INFORMATION

CME HARBORVIEW—Contact: Gayle Splater, Cytology Continuing Education, Dept. of Pathology, Harborview Medical Center, 325 Ninth Ave, Seattle, WA 98104. (206) 223-5953.

PCMS CME—Contact: Executive Director, College of Medical Education, 705 S Ninth, No. 203, Tacoma, WA 98405. (206) 627-7137.

U/W (UNIVERSITY OF WASHINGTON)—Contact: U/W School of Medicine, Div. of CME, SC-50, Seattle, WA 98195. (206) 543-1050.

VMMC (VIRGINIA MASON MEDICAL CENTER)—Contact: Linda Orgel, Division of Continuing Medical Education, Virginia Mason Medical Center, PO Box 900, Seattle, WA 98111. (206) 340-2058.

WSMA—Washington State Medical Association, Continuing Medical Education, 2033 Sixth Ave, Ste 1100, Seattle, WA 98121. (206) 441-9762.

OTHER CME OPPORTUNITIES

Brochures and registration forms are available from the contact person or organization listed at the end of each course or in the list of course sponsors and contact information.

STFM Family Conference. March 3–7, 1999. Kiawah Resort, Kiawah Island, South Carolina. Contact: Ray Rosetta, Meetings and Programs Director, Society of Teachers of Family Medicine, 8880 Ward Parkway, Kansas City, Missouri 64114. Phone (800) 274-2237, ext. 4512.

32nd Annual Spring Conference. April 28–May 2, 1999. Sheraton Seattle Hotel & Towers, Seattle, Washington. Contact: Ray Rosetta, Meetings and Programs Director, Society of Teachers of Family Medicine, 8880 Ward Parkway, Kansas City, Missouri 64114. Phone (800) 274-2237, ext. 4512.

35th Annual Forensic Dentistry. March 7–11, 1999. Holiday Inn, Silver Spring, Maryland. Credit 38 hrs. $300–$675. Contact: Ruth Murphy, CAME, Armed Forces Institute of Pathology, Washington, DC 20306-6000; (800) 577-3749 or (202) 782-2637; email: came@afip.osd.mil; www.afip.org.

58th Annual American Occupational Health Conference. April 23–30, 1999. Ernest N. Morial Convention Center, New Orleans, Louisiana. Contact: ACOEM Education Dept., 55 W. Seeger Road, Arlington Heights, IL 60005; (847) 228-6850 or fax (847) 228-1856; www.acoem.org.

80th Annual Session-American College of Physicians-American Society of Internal Medicine. April 22–25, 1999. Ernest N. Morial Convention Center, New Orleans. Credit 29 hrs. Contact: ACp-ASIM Customer Service (800) 523-1546, ext. 2600; www.acponline.org.

NOTICE

State Associations should send their CME listings for publication to:

Catherine Nancarrow, Editorial Manager
The Western Journal of Medicine
221 Main Street
San Francisco, CA 94120-7690

(415) 882-5177 • Fax (415) 882-3379 • rstraube@bmjgroup.com

Editorial

Children, Youth, and Families: Building on the Cultural Strengths of Hispanic and Latino Communities

Although we have an emotional commitment to improving the welfare of children, we have morbidity and mortality statistics that call into question the level of that commitment. More than 20% of children in the United States live in poverty, and millions do not have access to basic medical care. Approximately one third of all children are either unserved or underserved. Infant mortality is as high as 11% in some communities. Among certain groups of minority youth, death from homicide approaches 160 per 100,000.[1]

Although we tend to distinguish the statistical differences between ethnic groups, we should be aware of the substantial variations within these groups as well. For example, the Hispanic Health and Nutrition Examination Survey of 1982–1984 (HHANES) reports varying prevalences of medical, behavioral, and developmental disorders among different Hispanic or Latino groups. According to this survey, Puerto Rican children have a higher prevalence of asthma than Mexican American or Cuban American children. Mexican American and Cuban American children have higher birth weights than Puerto Rican children.[2] Thus, given the variations among populations, minorities should not be grouped into a single category for statistical purposes.

As a socially and culturally diverse nation, we face a major challenge: we must develop effective health-promoting strategies that address both the common etiologies of morbidity and unique, culturally specific, behaviors.

Representatives of diverse cultural groups, academicians, advocates, public officials, parents, and other professionals convened at Wingspread in Racine, Wisconsin, from June 28 to June 30, 1996. The Johnson Foundation, the Center for Children with Chronic Illness and Disability, and the University of Minnesota's Institute for Health and Disability in the Division of General Pediatrics and Adolescent Health jointly sponsored the meeting. The goal of *Children, Youth and Families: Building on Cultural Strengths of Hispanic and Latino Communities* was to exchange ideas about how to increase the cultural competence of health care professionals who serve children and youths with chronic conditions and how to improve the quality of the services provided to them. Several papers focusing on the assessment of health status, the impact of elevated asthma morbidity among Puerto Rican children, and the ethical and cultural considerations in working with diverse ethnic groups were commissioned.

Traditional health models hold that poverty is the major determinant of negative health outcomes. In *Latino Children's Health and the Family-Community Health Promotion Model,* Mendoza and Fuentes-Afflick[3] state that in most health models, poverty also impacts health status through environmental and behavioral factors. Starfield[4] found that poor children have morbidity rates for chronic and disabling conditions two to three times higher than those of non-poor children. Race and ethnicity are considered covariants in the relationship between poverty and health. Although we often focus on the negative effects of economically depressed environments, resiliency research has "shown that some aspects of the social-environmental milieu may serve as a buffer against the negative effects of poverty." Mendoza and Fuentes-Afflick present a compelling proposal that challenges traditional health models and invites the reader to consider a new health model, one which incorporates both the medical and public health perspectives.[3]

Mendoza and Fuentes-Afflick postulate that health care professionals should place greater emphasis on the interrelationships between individuals and the family-community complex, as opposed to the genetic-behavioral-environmental triad accented by more traditional health models. They explain that families have the capacity to support the beneficial health behaviors of their members and to make effective use of the natural supports found in their immediate communities. Mendoza and Fuentes-Afflick propose that health status should be assessed from a perspective that considers physical and psychological health, factors that contribute to understanding an individual's functional status, in addition to social and environmental conditions.

In a detailed review of the literature on Hispanic youths with asthma, Lara and collegues[5] report that asthma occurs in 11.2% of mainland Puerto Rican children, 2.7% of Mexican American children, 5.9% of non-Hispanic, black children and 5.2% of Cuban American children. Other genetic and biologic risk factors include possible differences in inflammatory responses, differences in airway size, premature birth, and low birth weight. Lara and collegues also mention socioenvironmental factors as possible factors in the development and expression of the disease. They present access to health as a major problem for Latino children and their families. Barriers to access included language, cultural issues, difficulty obtaining follow-up appointments, and the inability to see a primary care physician.

Lara and colleagues' paper raises provocative questions about research and policy, questions that should trigger the interest of investigators, academicians, and public health activists and compel them to explore the risk and prognostic factors that influence diverse ethnic groups.

In summary, these two papers challenge current methods for measuring health status and propose an alternative health promotion model, one that takes into account the individual's, family's, and community's perceptions

and interpretations of health status or quality of life. Research questions are posed to instigate further investigation of the influence that ethnicity and culture have on health status and health care policy development.

Many recommendations emerged from the conference dialogues around these papers. They addressed service delivery and systems issues; training of professionals, families, and policy makers; and research. Highlights of these recommendations appear below:

There is a need to emphasize multidisciplinary and collaborative strategies in improving systems of care and service delivery. This includes participation in planning, organizing, and delivering services by families, community institutions (health services, education, and social services) and voluntary community associations (churches, neighborhoods, and peer networks). It also includes a focus on the safety of the physical environment in which families live so that risks can be reduced. This process will improve the understanding of the health care needs of these populations.

There is a need in training and practice to focus on understanding unique family strengths and what they contribute to a family's well-being. Understanding the influence of socioenvironmental and cultural factors on a family's health beliefs and practices, organization, and patterns for accomplishing roles will provide practitioners with improved understanding about the family's expectations and level of parental knowledge and experience. With this knowledge, practitioners can more ably tailor treatment decisions to foster best outcomes.

There is a need to conduct research using multiple methods (interviews, videotapes, self-report, participant observation) grounded in the real lives of families that emphasize the different stages of family development (immigrant or first generation, living in rural or urban environments, primary language), with a focus on children with chronic conditions. This research will provide information to increase understanding about developmental pathways and the effects of chronic stressors such as poverty and violence; it will also lead to improved service delivery.

Acknowledgment

Funding for the Building on Cultural Strengths conferences and these papers was provided by a grant from the Maternal and Child Health Bureau, Health Resources Administration #MCJ-279409-02-0.

JAVIER ACEVES, MD
Clinicol Associate Professor of Pediotrics
University of New Mexico, HSC-SOM
Albuquerque, New Mexico

REFERENCES

1. Hennes H. A review of violence statistics among children and adolescents in the United States. Pediatr Clin North Am 1998; 45:269–291

2. Fuentes-Afflick E, Lurie P. Low birth weight and Latino ethnicity: Examining the epidemiologic paradox. Arch Pediatr Adolesc Med 1997; 7:665–674

3. Mendoza FS, Fuentes-Afflick E. Latino children's health and the family–community health promotion model. West J Med 1999; 170: 85–92

4. Starfield B. Childhood morbidity: Comparisons, clusters, and trends. Pediatrics 1997; 88:519–526

5. Lara M, Morgenstern H, Duan N, Brook R. Elevated asthma morbidity in Puerto Rican children: a review of possible risk and prognostic factors. West J Med 1999; 170:75–84

Articles

Elevated Asthma Morbidity In Puerto Rican Children: A Review of Possible Risk and Prognostic Factors

MARIELENA LARA, MD, MPH; HAL MORGENSTERN, PHD; NAIHUA DUAN, PHD; *and* ROBERT H. BROOK, MD, SCD; *Los Angeles, California*

Latino children represent a significant proportion of all US children, and asthma is the most common chronic illness affecting them. Previous research has revealed surprising differences in health among Latino children with asthma of varying countries of family origin. For instance, Puerto Rican children have a higher prevalence of asthma than Mexican American or Cuban American children. In addition, there are important differences in family structure and socioeconomic status among these Latino populations: Cuban Americans have higher levels of education and family income than Mexican-Americans and Puerto Ricans; mainland Puerto Rican children have the highest proportion of households led by a single mother. Our review of past research documents differences in asthma outcomes among Latino children and identifies the possible genetic, environmental, and health care factors associated with these differences. Based on this review, we propose research studies designed to differentiate between mutable and immutable risk and prognostic factors. We also propose that the sociocultural milieus of Latino subgroups of different ethnic and geographic origin are associated with varying patterns of risk factors that in turn lead to different morbidity patterns. Our analysis provides a blueprint for future research, policy development, and the evaluation of multifactorial interventions involving the collaboration of multiple social sectors, such as health care, public health, education, and public and private agencies.

(Lara M, Morgenstern H, Duan N, Brook R. Elevated asthma morbidity in Puerto Rican children: a review of possible risk and prognostic factors. West J Med 1999; 170:75–84)

Health status, use of health services, and socio-demographic attributes vary among subgroups of Latino children. For example, the 1982–84 Hispanic Health and Nutrition Examination Survey (HHANES) revealed that mainland Puerto Rican children have higher rates of asthma (11.5%), psychological and behavioral problems (5.7%), speech problems (6.7%), and mental retardation (3.1%) than Mexican American and Cuban American children.[1] The 1989–1991 National Health Interview Surveys (NHIS) indicated that mainland Puerto Rican children had the highest average number of annual bed days due to illness (9 annual bed days), followed by Mexican American children, then Cuban American children who did not differ from non-Latino white children (6 annual bed days).[2] Puerto Rican children, who are both the poorest of all children in the United States and the sickest among Latino children,[3] also had the highest average number of doctor visits of all US children (13 doctor visits per year). In comparison, one quarter of Mexican American children did not visit a doctor at least once a year, and poor children of Mexican origin spent fewer days in bed than their non-poor counterparts.[2] These differences in disease prevalence and health outcome suggest that specific patterns of risk factors may vary by Latino subgroup.

In 1990 in the United States and Puerto Rico, 13% of children younger than 15 were of Latino origin. An estimated half million Latino children had asthma symptoms, two-thirds of whom were of Puerto Rican origin.[4–7] In this paper, we use asthma as a model to explore differences in morbidity among Latino children. In particular, we review what is known about asthma morbidity among Latino subgroups; identify risk and prognostic factors that may explain these differences,

From the UCLA/RAND Program on Latino Children with Asthma, Division of General Pediatrics, UCLA Department of Pediatrics (Dr Lara), and RAND Health (Drs Lara, Duan, and Brook), and from the Center for Occupational and Environmental Health, Department of Epidemiology, UCLA School of Public Health (Dr Morgenstern), Los Angeles, California.

Reprint requests to Marielena Lara, RAND Health, 1700 Main Street, PO Box 2138, Santa Monica, CA 90407-2138 (e-mail: lara@rand.org).

placing special emphasis on those factors that are mutable or amenable to intervention; and discuss the research, clinical, and public health implications of these differences in morbidity.

Definitions

Asthma Prevalence and Morbidity

Past studies have measured prevalence rates for asthma, or the proportion of a population having the condition, using reports of asthma symptoms or physician diagnosis and the time period for which prevalence is estimated. Wheezing is the asthma symptom on which most prevalence estimates are based. Prevalence can be considered in two time periods: ever asthma, referring to lifetime or cumulative prevalence, and active asthma, referring to point or period prevalence. Ever asthma refers to children whose parents have been told that the child has asthma, but who have not had any symptoms or impairment in the last year. Active asthma refers to children whose parents have been told that the child has asthma and who have experienced symptoms or impairment within the last 12 months.

Morbidity level, on the other hand, refers to the degree to which a child with active asthma experiences symptoms or pulmonary and functional impairment. In characterizing morbidity level, three dimensions are important: control of asthma symptoms, functional status, and quality of life. Asthma control refers to the frequency and intensity of asthma symptoms and variations in objective measures of pulmonary function. Functional status refers to the degree to which asthma affects the physical, mental, and social function of the child, such as the number of school and activity days lost as a result of asthma. Lastly, quality of life refers to the perception of impairment, in that the children or parents may perceive children with the same level of symptoms and number of school days lost to be impaired to different degrees. Previous research also indicates that the report of symptoms and the perception of impairment can differ by reporter, or parent versus child,[8–9] and by ethnicity, for instance Latino versus non-Latino.[10]

Latino Ethnicity

People of Latino ethnicity can differ by country of origin and place of residence. Puerto Ricans are either born on the island of Puerto Rico (island Puerto Ricans) or in the continental United States to parents born in Puerto Rico or of Puerto Rican ancestry (mainland Puerto Ricans). Because migration between the island and the mainland is common, island and mainland Puerto Ricans can also be identified by place of past and current residence. Island Puerto Ricans are US citizens by birth. Mexican Americans are either born in the Unites States to Mexican born parents or are naturalized immigrants from Mexico. Similarly, Cuban Americans may have been born in the United States or may be naturalized Cuban immigrants. Because place of birth and early life residence may be risk factors for asthma, it is important to define Latino ethnicity as specifically as possible.

Differences in Asthma Prevalence and Morbidity

Research indicates that asthma prevalence rates vary among subgroups of Latino children, but little is known about differences in morbidity. Table 1 summarizes key studies indicating that mainland and island Puerto Rican children have the highest asthma prevalence of all Latino and non-Latino children in the United States.

Using data from HHANES, Carter-Pokras and Gergen[6] estimated a point prevalence of asthma for Mexican American children (2.7%) similar to that of non-Hispanic white children (3.3%), but much lower than that of mainland Puerto Rican children (11.2%), non-Hispanic black children (5.9%), and Cuban American children (5.2%). Lifetime prevalence of asthma was 20.1% among mainland Puerto Rican, 8.8% among Cuban American, and 4.5% among Mexican American children.

Two additional studies corroborate the high prevalence of asthma among mainland Puerto Rican children. In the Bronx, New York, where most Latino children are mainland Puerto Rican, Crain[11] found that the 12-month period prevalence of asthma was 10% among Hispanic children, as compared to 6.9% among blacks and 7.6% among whites. Lifetime asthma prevalence was 17.9% among Hispanic, 11.6% among black, and 8.2% among white children. These ethnic-specific differences in prevalence persisted after controlling for income and were based on a random-digit parent telephone survey. In Connecticut, where Hispanics are mostly Puerto Rican, Beckett[12] reported a lifetime asthma prevalence of 18.4% among children of Hispanic mothers, compared to a lifetime prevalence of 11.3% among blacks and 7.4% among whites. These prevalence estimates were based on maternal reports in a statewide representative sample of English-speaking women who had recently given birth. The increased risk for physician-diagnosed asthma among Hispanics in this data set persisted after controlling for socioeconomic status and active smoking in the home.

Orengo[7] has also described very high prevalences of asthma among children on the island of Puerto Rico. Investigators used a parent and adolescent population-based school survey that followed the protocol of the International Study of Asthma and Allergies in Child Health (ISAAC).[13] They found that the lifetime prevalence of asthma was about 50% for 6-to 7-year-olds, as reported by their parents, and about 30% for 13- to 14-year-olds, as reported by themselves. In addition, about one third of 6- to 7-year-olds and about one quarter of 13- to 14-year-old island Puerto Rican children had had symptoms of asthma in the last year. The investigators conducted the above study in two towns in Puerto Rico, the industrial town of Cataño, where the community suspected asthma problems to be associated with high air pollution levels,

TABLE 1.—*Studies Estimating the Prevalence of Asthma Among US Latino Children: 1993–1996*

Source	Age	Location	Ethnicity	Lifetime Prevalence: Ever diagnosed? (%)	Lifetime Prevalence: Ever wheezed? (%)	Period Prevalence: Had asthma in the last 12 months?(%)	Period Prevalence: Wheezed in the last 12 months?(%)
Carter-Pokras[6] (1993)	6 months–11 years	New York City	Mainland Puerto Rican	20.1	—	11.2*	—
		Southwest Miami	Mexican American	4.5	—	2.7*	—
			Cuban American	8.8	—	5.2*	—
			Non-Hispanic black	9.1	—	5.9*	—
			Non-Hispanic white	6.4	—	3.3*	—
Crain[11] (1994)	0–17 years	New York City	Hispanic†	17.9	—	10.0	12.9‡
			Black	11.6	—	6.9	12.7‡
			White	8.2	—	7.6	14.0‡
Orengo[7] (1996)	6–7 years	Puerto Rico	Island Puerto Rican	45–47§	48–51‡§	—	29–33‡§
	13–14 years			25–28§	34–39‡§	—	23–25‡§
Becket[12] (1996)		Connecticut	Hispanic†	18.4	—	—	—
			Black	11.3	—	—	—
			White	7.4	—	—	—

*Refers only to patients with active asthma or having asthma when interviewed (point prevalence).
†Mostly mainland Puerto Rican.
‡Includes children who wheezed but did not necessarily have a diagnosis of asthma.
§Range reflects prevalence estimates for the town of Cataño and a control town in Puerto Rico.

and a control town. No appreciable differences in asthma prevalence were found between the two towns.

Other differences in asthma morbidity among Latino children have not been studied in national population-based samples. Data from clinical settings, however, indicate that Latino children experience significant asthma morbidity. Of Mexican American children with moderate to severe asthma who attended an outpatient clinic in Texas, 67% had been hospitalized previously, and 74% had experienced at least an occasional limitation in their ability to play. These children also missed an average of 13 days of school per year because of asthma.[14] The results of the National Collaborative Inner-City Asthma Study (NCICAS) indicated that significant asthma morbidity occurred in Latino children, who formed about 20% of the total sample. They were predominantly mainland Puerto Rican children living in New York City or mainland Puerto Rican and Mexican American children living in Chicago. The 291 Latino children included in the NCICAS sample had experienced an average of 3.7 days of wheezing during the previous two weeks, compared to an average of 3.2 days experienced by African American children ($P < 0.01$).[15] After comparisons between Latino and African American children were adjusted for the two cities where most Latino children lived, Chicago and New York, this difference in morbidity was no longer statistically significant in this small study sample.

Data on childhood asthma prevalence and morbidity in Latino subgroups are limited by possible measurement errors associated with differences between studies to date in selection methods, participation rates, and definitions of both asthma and Latino ethnicity. Studies have not reported consistent findings with regard to the effect of socioeconomic status on morbidity. Although asthma is probably caused by multiple risk factors, most research to date has observed only bivariate (crude) comparisons between asthma and one risk factor. In spite of these methodological limitations, the observed differences in prevalence are particularly large. We will review possible risk and prognostic factors that can be applied in future research to explain the above differences, although these factors have been identified in mostly non-Latino populations.

Differences in Risk and Prognostic Factors

Table 2 presents a conceptual summary of the possible risk and prognostic factors for asthma prevalence and morbidity that we have identified through a review of the scientific literature and clinical experience. For the purposes of this discussion, we distinguish between risk and prognostic factors. *Causal risk factors* are positively associated with incidence of disease, *protective risk factors* are negatively associated with incidence of disease, and *prognostic factors* affect the disease's morbidity and remission, once it has occurred. Research to date, however, has not completely clarified whether certain factors are risk factors, prognostic factors, or both.

Before discussing risk and prognostic factors, it is important to keep in mind which are *mutable*, or given the current state of scientific knowledge, potentially modifiable through interventions. *Immutable* factors are very difficult, if not impossible, to modify. Classifying a factor as mutable or immutable in this scheme depends on the perspective of the intervention. From a traditional

TABLE 2.—*Possible Childhood Asthma Risk and Prognostic Factors*

Type	*Genetic/Biologic*	*Physical Environment*	*Social Environment*
Mutable (amenable to intervention)	Low birth weight	Home exposures Early life Current Some outdoor exposures	Health care Screening Treatment Family & Community Support mechanisms Behaviors & beliefs
Immutable (very difficult to modify)	Ethnic ancestry Race Immune predisposition	Past home exposures Some outdoor exposures	Socioeconomic conditions Family psychosocial stressors

medical perspective, for instance, one would consider as immutable any factor over which the health care and public health care systems have no control. Examples include outdoor pollution and socioeconomic stressors, such as poverty and inappropriate housing.

Genetic Predisposition and Other Biologic Factors

Researchers currently regard asthma, the presence of recurrent but reversible respiratory obstruction symptoms, such as cough and wheezing, as a chronic inflammatory disorder of the airways[16] that can have a strong allergic and hereditary component.[17–20]

Preliminary research suggests that genetically determined differences in inflammatory response, particularly those related to the substance alpha-antitrypsin, may exist in Puerto Rican children with asthma. Genetic studies have shown that people with asthma can have an abnormal variant of alpha-antitrypsin (AAT), a protein related to inflammatory reactions and, more specifically, they can have elevated levels of the S or Z variant.[21] Studies in the Bronx have shown that the increased incidence of asthma among mainland Puerto Rican adults and children is associated with AAT variant phenotypes.[21–22] Although abnormal variants of AAT are unlikely to be solely responsible for the higher prevalence of asthma among Puerto Rican children, genetic differences may account in part for this difference.

Differences in the predisposition of Latino children to asthma may also be associated with two other physiologic factors can either be determined or exist at birth. These factors include differences in airway size and premature birth or low birth weight. One hypothesis for future study is that differences in asthma outcomes among Cuban American, Mexican American, and Puerto Rican children may be related to differences in airway size. Hsu[23] and Dodge[24] found that Mexican American children had better lung function than a comparison group of white or non-Mexican American children and speculated that the lower prevalence of asthma among Mexican Americans could be associated with larger airways that are less likely to wheeze.

Oliveti[25] has shown an association between asthma prevalence and prematurity and low birth weight among inner-city African American children. This association has yet to be studied with regard to Latino children. The differences in birth weight distribution among Latinos, however, are well described,[1,26] with Mexican American and Cuban American children having higher birth weights than Puerto Rican children. These differences suggest that prematurity and low birth weight may also be risk factors for asthma among specific subsets of Latino children.

Differences in the Physical and Social Environment

In addition to genetic and physiologic factors, environmental and social factors have been implicated in both the development of asthma and the exacerbation of its symptoms. Research indicates that, among mostly non-Latino populations, the physical and social environment can affect both the development and expression of the disease. The effects of the physical environment include indoor or home exposures to such allergens as molds or pets and outdoor exposures to allergens like air pollution or pollens. The social environment's influence involves the behaviors, beliefs, and structure of the immediate family unit, as well as those of the community and social culture in which the family operates.

Indoor and Outdoor Exposures

Exposures early in life to indoor allergens, such as cockroaches, can be associated with both the development of asthma and a greater occurrence of asthma symptoms.[27,28] Preliminary data from NCICAS indicate that, compared with African American children, Latino children have a greater proportion of positive skin tests, which indicate abnormal allergic and inflammatory responses to indoor allergens.[15] In a sample of mostly Mexican American children hospitalized for asthma in Los Angeles, Richards[29] found that few families were instituting measures to avoid allergens in the home. Control of indoor or home asthma-aggravating environmental triggers is critical to the appropriate management of the illness.

Research has yielded conflicting scientific evidence of the connection between asthma and air pollution. Some studies have described an association between daily air pollution levels and asthma symptoms, emergency room visits, and hospitalizations.[29–31] Orengo,[7] however, did not find a relationship between outdoor environmental pollutants and asthma prevalence on the island of Puerto Rico. The interpretation of some of these studies is difficult because of their ecological nature; they do not directly compare exposures. Possible differences, however, in the acute effects on symptoms and the chronic effects of air pollution have been described.[32]

Differences in Family Structure and Community

The results of several studies suggest that differences in family behaviors, beliefs, structure, and function are associated with asthma morbidity. Parental smoking is a key behavior associated with asthma. Several studies in non-Latino populations have shown that children exposed to smoking are more likely to develop asthma.[25,33,34] Differences in smoking behaviors among Latinas may be associated with different asthma outcomes for their children. The Hispanic Health and Nutrition Examination Survey showed that Puerto Rican women have the highest rate of smoking. Of Puerto Rican women between 12 and 49 years old, 32% smoke, compared to 23% of Cuban American and 21% of Mexican American women.[35] Puerto Rican teenage girls have the highest prevalence of smoking: 16% of Puerto Rican teenage girls reported that they smoke, compared to 9% of Mexican American and 6% of Cuban American teenagers.[36] Thus, a hypothesis for future research is that the higher prevalence of asthma among Puerto Rican children is associated with a higher prevalence of maternal smoking, particularly among teenage mothers. The effects of passive smoking and the indirect effect of smoking during pregnancy on intrauterine development may both influence the child's asthma risk.

Family beliefs regarding asthma and the efficacy of medical treatment can influence such health behaviors as seeking care and compliance with prescribed regimens. Scrimshaw[37] reported an ethnographic study of Mexican Americans who viewed asthma as a disease for which conventional medical regimens are effective, but who considered ethnomedical rituals more effective in the treatment of seizures. Mainland Puerto Rican families sometimes treat asthma with folk or home remedies, which include rubbing the chest with oils and Vicks preparations, but almost all of them use medications or seek traditional medical care when a child has an asthma attack.[38,39] When explaining differences in asthma prevalence and morbidity, it is important to consider ethnic-specific cultural beliefs and perceptions of illness, but not to the exclusion of universal health beliefs and behaviors that may be more central to the health issues and problems families encounter.[38]

Research conducted among mostly non-Latino populations suggests that differences in family structure and function can affect the exacerbation of asthma symptoms,[40] adherence to medical regimens,[41–43] hospitalization,[44] and mortality[45] in children with asthma. In addition, some evidence suggests that exposure to a stressful family environment early in life can be associated with the development of asthma among genetically predisposed individuals.[43]

Documented differences in family and community structure among Latinos may be associated with better asthma outcomes in Mexican Americans. Protective social factors may include the higher prevalence of two-parent households among Mexican Americans and Cuban Americans, as compared to the higher rate of single motherhood among mainland Puerto Ricans.[3] The concept of "familismo," the presence and importance of extended family support structures among Mexican Americans,[46] and the emphasis placed on higher education by Cuban Americans, could also be associated with an enhanced capacity to cope with the multiple demands of having a child with a chronic disease.

Another important aspect of the social environment that research on children with asthma has not emphasized is the evaluation and management of psychiatric comorbidities. Two national studies have documented the high prevalence (about 35%) of behavioral problems in children with asthma.[47,48] A high prevalence of depression exists among mothers of inner-city children, particularly among mothers of children with asthma.[41,48] Emerging research indicates that undiagnosed and untreated depression is a major health issue for Latinas (K. Wells, MD, MPH, oral communication, September 1998).

Access to Health and Public Health Care Services

Because appropriate medical care can control asthma symptoms,[16] the quality of health care services and access to them are important determinants of outcome. Indicators of access to care include the presence of barriers to care, such as the lack of insurance, and the use of asthma services when the child needs them.[49,50] The quality of asthma care depends on structural and process requirements for good asthma care, such as ensuring specialty training for the health care provider, maintaining an inventory of necessary equipment and medications, and providing the family with adequate asthma education and instruction for care.[50,51] In addition, adequate coordination with community-based organizations, such as schools, is crucial when working with children and families to reduce asthma morbidity. The community and the various parts of the health care and public health care systems need to work together to help families resolve asthma-related issues.

Accessing health care is a major problem for Latino children and their families; Latino families have a lower rate of health insurance than other minority groups[52] and experience additional language and cultural barriers to health care.[53,54] Finkelstein[55] found that Latino preschoolers hospitalized for asthma were less likely than white children to receive maximal preventive therapy prior to hospital admission or to obtain equipment to help manage asthma after discharge. Preliminary results of NCICAS indicate that inner-city children with asthma

experience significant barriers to care. Although about 95% of inner-city children with asthma reported having a regular place for attack or follow-up care, nearly half had difficulty obtaining follow-up care, about 25% experienced a long wait for an appointment, and 20% could not see their own doctor.[56,57] More research is necessary to evaluate the accessibility and quality of care for children with asthma, as well as the relation of both to the level of morbidity among different groups of Latino children.

Research Implications

This paper has examined what is known about why children of Latino backgrounds have different prevalences of asthma. This review raises two questions. Why do Puerto Rican children have the highest prevalence of asthma among all Latino and non-Latino children in the United States? Why do Mexican American children, in spite of poverty and lack of access to care, appear to have a lower prevalence of asthma than Puerto Rican children?

Research Hypotheses

Our overarching hypothesis is that Puerto Rican children have higher prevalence of and morbidity from asthma because of an interaction of genetic predisposition and exposure to social and physical environmental risk factors.

Testing this hypothesis should involve a step-wise approach. First, bivariate analyses should test for main effects or major risk factors associated with an increased prevalence of asthma. Second, multivariate analyses should test for secondary or combined effects. A multivariate approach can control for confounding or bias, examine possible interaction effects, and "explain" ethnic differences in terms of specific risk and prognostic factors for asthma.

We propose the following five hypotheses to evaluate differences in the prevalence and morbidity of asthma between Latino and non-Latino children and between subgroups of Latino children. First, we propose that children of Puerto Rican ancestry have a higher genetic or biologic predisposition to asthma. Research to date indicates that Puerto Rican children have a higher prevalence of asthma than Mexican American, Cuban American, and other non-Latino children. It is likely that these differences are attributable in part to differences in the immune predisposition to asthma among Latinos. Thus, the first main effect to test is ethnic ancestry or family country of origin, because ethnic differences may be attributed to unmeasured genetic or biological factors.[58,59]

As a second hypothesis, we propose that the higher prevalence and morbidity of asthma in poor children is associated with multiple poverty-related risk factors. Asthma prevalence is higher among poor US children.[60] Poverty is associated with such risk and prognostic factors for asthma as poor access to care, detrimental home exposures, and unstable family structures. Although research has shown the independent effects of these factors, we need to investigate whether these factors have a greater effect when they occur simultaneously. The lower prevalence of asthma in Cuban American children may be due to a positive association between protective risk factors and socioeconomic status, measured by parental education and income. On the other hand, Puerto Rican children have the highest morbidity from asthma and are also the poorest in the United States.[3] Therefore, the effects of poverty and its related risk factors need to be researched.

Third, we propose that Puerto Rican, Mexican American, and Cuban American families have different family structures and related social risk factors. The association between poverty and higher incidences of asthma among Puerto Rican children and between a lack of poverty and lower incidences of asthma among Cuban American children does not hold for Mexican American children. One possible explanation is that Mexican American children have a lower frequency of social risk factors, such as single-parent households, relative to Puerto Rican children. In addition, migration may be associated with positive or negative risk factors. Immigrants may have higher socioeconomic status than residents of their country of origin and more resilient behaviors, such as seeking out the best possible access to health care for their children. For example, it is possible that Puerto Rican children born and raised on the island of Puerto Rico have a higher asthma morbidity than mainland Puerto Rican children born and raised in the continental United States. Yet, immigration may also be associated with negative risk factors, such as a lack of social or extended family support. Thus, the combined effects of family risk factors and ethnicity need to be studied.

Fourth, we propose that poor children of Puerto Rican ancestry have a higher prevalence of asthma than nonpoor Puerto Rican children. This hypothesis tests whether poverty and its associated risk factors compound the risk associated with country of origin and genetic ancestry. Because most Puerto Rican children with asthma are poor, the observed differences among ethnic groups are likely to result from the combined effect of these factors.

Finally, we propose that Puerto Rican, Mexican American, and Cuban American families have different migration patterns and reside in US geographic sites associated with different physical and social environmental exposures. Latino children of different backgrounds are unevenly distributed across the United States. Most Puerto Rican children live on the island of Puerto Rico or in the Northeast and Illinois, with the largest mainland concentrations residing in New York City, Chicago, and Philadelphia. Most Mexican American children live in the Southwest, or in Los Angeles and Houston, although a significant number also live in Chicago. Most Cuban American children live in Miami.[10,61] Thus, we need to study whether the main effect of Latino ethnicity or genetic ancestry may be partially explained by location and whether location may in turn be partially explained by environmental factors. For example, higher morbidity in mainland Puerto Rican children may be related to living in

impoverished neighborhoods of New York City with high levels of outdoor pollution and crowded inner-city home environments conducive to asthma.

Research Strategies

We propose that future research should use available national epidemiological databases to test preliminary hypotheses as to the effects of some of the identified risk and prognostic factors. Research should also evaluate the relative contribution of all important risk factors through longitudinal observational studies, identify the mutability of some risk factors through intervention, and evaluate the cost-effectiveness of multi-component interventions. In addition, research would be enhanced by the use of measures shown to be reliable and valid in non-English-speaking populations of varied cultural backgrounds.

The previously listed hypotheses cannot be tested using currently available information; however, population-based databases, such as the annual National Health Interview Survey, could be used to explore the role of some of the identified risk factors. These databases are representative of the US population and can be used to compare asthma prevalences between Latinos and non-Latinos, as well as among Latinos of the same country of origin living in different geographic locations in the United States. The risk factors accounted for by these databases are limited to self-identified ethnicity and to some indicators of access to care and socioeconomic status. Yet, the available population-based information can be used to estimate the relative importance of risk factors. In addition, using data from multiple years both increases sample size and facilitates the uncovering of time trends in asthma prevalence.

Longitudinal cohort studies are necessary for a more in-depth evaluation of the risk and prognostic factors associated with the incidence and remission of asthma. Prospective observational data can help determine whether risk factors are positive (causal) or negative (protective) with less potential bias than data from cross-sectional studies. The more detailed information obtained by such studies allows for the determination of patterns among the risk factors and for more extensive testing of combined and interaction effects. For example, rather than measuring ethnicity and geographic location solely by self-identified ethnicity, these effects can be measured in multiple ways, for instance by parent's place of birth and residence, child's place of birth, and child's early life and current residences. Physiologic markers, such as genetic markers and pulmonary function, can be measured. More specific information regarding the accessibility and quality of care can be obtained. Yet, following procedures to assure that samples are representative and tracking subjects longitudinally can be very time-consuming and expensive.

Intervention research can provide information regarding the mutability of risk and prognostic factors. Given that asthma is most likely a multifactorial illness, intervention research can help determine empirically which factors are most important in preventing asthma and reducing its morbidity. Intervention studies can be directed at single risk factors or "bundled" to reduce multiple risks simultaneously. Research to date suggests that single medical and educational interventions to treat asthma can reduce morbidity.[62,63] Additional intervention research would provide information about the relative contribution of home environmental risk factors. At present, however, a multifactorial intervention that accounts for changes in health care, as well as for social and physical environmental factors, has yet to be conducted so that the independent and combined effects of these factors on asthma outcomes can be rigorously determined.

In particular, research is needed that develops and evaluates interventions to modify risk and prognostic factors among Latino children and their families. These interventions would aim to improve mental, physical, and functional health.

Clinical and Public Health Implications

Basic research questions regarding the relative contributions, possible interactions, and mutability of the multiple risk factors discussed above undoubtedly remain unanswered. Regardless of the cause of asthma, however, a gap exists between the current capacity to treat the condition and the availability of medical therapies in real world settings, particularly among underserved populations. Clinicians and public health officials can take steps to reduce this avoidable gap in the morbidity of asthma between Latino and non-Latino children.

The individual clinician can be aware of the increased morbidity among Puerto Rican children and of the environmental risk factors associated with increased morbidity in both these and other children. He or she can make a special effort to keep up-to-date on high quality asthma medical management. The clinician can take additional steps when treating high-risk patients, such as monitoring changes in clinical status, modifying medical therapy more frequently, and facilitating the elimination of detrimental home exposures.

Public health programs for asthma prevention and control are essential given the magnitude of the problem, particularly among Puerto Rican children. Table 3 lists a range of possible primary, secondary, and tertiary prevention strategies.

Multiple sources of evidence, based primarily on studies of non-Latino children, indicate that morbidity from asthma in children that already have the condition can be reduced through tertiary prevention. Home environments can be modified to reduce or eliminate ongoing detrimental physical exposures, such as tobacco smoke, cockroaches, and mites. The health care available to all children with asthma can be improved to include appropriate medical evaluation and drug therapy by a regular provider. The child and his or her family can be educated, so that they can better manage the child's asthma care. The personal health system, the public health system, and community-based organizations,

TABLE 3.—*Possible Childhood Asthma Prevention Strategies*

Strategy	*Primary*	*Secondary*	*Tertiary*
Health care			
Screen for children at risk for asthma	✓	✓	
Provide early treatment			
For children at risk		✓	
For children diagnosed with asthma			✓
Improve continuous access to quality care			
Provide medications and equipment		✓	✓
Asthma education		✓	✓
Mental health services for high-risk families	✓	✓	✓
Physical environment			
Reduce early life home exposures for children at risk	✓	✓	
Eliminate current home exposures		✓	✓
Reduce outdoor exposures	✓	✓	✓
Social environment			
Provide financial and other support to high-risk families	✓	✓	✓

such as schools and churches, can establish partnerships for care to support the families of children with asthma.[16] In addition, some evidence suggests that promoting protective social factors, such as close-knit family structures, and ameliorating social risk factors, for instance, by treating psychiatric comorbidities, can also decrease childhood asthma morbidity.[43]

Secondary prevention strategies refer to the early detection and treatment of possible asthma among children who have a genetic predisposition or early signs of the illness. Such strategies would include implementing public health programs geared toward identifying genetic predisposition to asthma early in life, providing early preventive medication therapies, and eliminating or diminishing such exposures in the physical environment as second-hand smoke and cockroaches and such exposures in the social environment as parental mental health problems.

Primary strategies for the prevention of asthma among children are speculative, given the current state of the art. These strategies include screening for genetic predisposition, based on ethnicity or other genetic markers that have yet to be determined, and avoidance of conditions conducive to asthma. For example, preliminary research suggests that eliminating detrimental home exposures and providing mental health and other supportive services to high-risk families can prevent children with a predisposition to asthma from developing early signs of the illness.[43]

Population-based approaches need not only to address risk and prognostic factors, but be cost-effective and feasible as well. Current evidence suggests that health care and non-health-care factors are important and need to be addressed for effective disease control. Thus, we need to develop and evaluate public health interventions that go beyond the activities solely under the control of the traditional health care system. It appears that collaborative efforts with schools, environmental and housing agencies, and other community-based organizations are necessary to the support of families in the management of a given child's illness and the elimination of physical environmental exposures conducive to the development of asthma.

Policymakers and analysts evaluating these kinds of programs are also concerned with the equity and efficiency of effective programs. They are interested in evaluating the equity of programs that decrease morbidity across the whole population by ameliorating the disproportionate presence of mutable risk factors in high morbidity populations. Because they have limited resources to meet this goal, however, they are also interested in efficient programs that intervene in areas where the greatest reduction in morbidity is gained at the lowest possible cost.

Summary

The elevated morbidity of asthma among Puerto Rican children has important implications for clinical research and public policy. The clinician taking care of patients needs to be aware of differences in morbidity and take additional steps to optimize medical management for all children, but especially for those in high-risk families. The research community can use asthma in this population as a model to study asthma risk and prognostic factors, as well as the probable interaction of genetic and environmental influences. From a public policy perspective, population-based prevention and treatment programs, together with surveillance systems to track differences in morbidity, are necessary.

Asthma is the most common chronic illness affecting children. It affects Latino children differentially and is amenable to medical and environmental intervention. Latino children with asthma serve as a good example of

how ethnic-specific differences in risk and prognostic factors can generate substantial differences in the patterns of disease observed between populations. The issues outlined in this paper are not particular to Latinos or to children with asthma and can be applied to any ethnic group with a distinct genetic, geographic, and cultural identity. Lessons learned from this kind of research can help us frame similar questions regarding the physical, mental, and functional health of other Latino and non-Latino children with chronic illnesses. Research and policies related to the health of ethnically diverse populations should be based on robust models that account for the effect of the sociocultural milieu on health.

Acknowledgments

The authors thank Fernando Mendoza, Elena Fuentes-Afflick, and Glorisa Canino for the scientific discourse that led to the development of this paper. This work was funded by the Robert Wood Johnson Foundation, the Agency for Health Care Policy Research, the Bureau of Maternal and Child Health, the UMHC Center for Chronic Illness and Disability, the UCLA Department of Pediatrics, and RAND Health.

REFERENCES

1. Mendoza FS, Ventura SJ, Valdez RB, et al. Selected measures of health status for Mexican-American, Mainland Puerto Rican, and Cuban-American children. JAMA 1991; 265: 227–232

2. Flores G, Bauchner H, Feinstein AR, Nguyen UDT. The impact of ethnicity, family income, and parental education on children's health and use of health services. Am J Public Health 1999; (In press)

3. Bureau of the Census. Selected social characteristics of all persons and Hispanic persons by type of origin: March 1997. Available at: htpp://www.census.gov/population/hispanic/cps97.

4. Garcia JM, Montgomery PA. The Hispanic population in the United States: March 1990. Washington, DC, US Bureau of the Census, Current Population Reports publication No. P20-449, 1991

5. 1990 Census of Population: General Population Characteristics of Puerto Rico. Washington, DC, US Bureau of the Census, Current Population Reports publication No. CP-1-53, 1992

6. Carter-Pokras OD, Gergen PJ. Reported asthma among Puerto Rican, Mexican-American, and Cuban children, 1982 through 1984. Am J Public Health 1993; 83: 580–582

7. Orengo JC, Loyo NI, Serrano RA, Mercado HE, Horta H. Prevalence of Respiratory and Allergic Problems Among School-Aged Children in the Air Basin. Presented at the Cataño Workshop of the Puerto Rican Department of Health, Environmental Health Secretariat and the US Environmental Protection Agency, San Juan, Puerto Rico, 1996

8. Lara M, Duan N, Sherbourne C, et al. Differences between child and parent reports of symptoms among Latino children with asthma. Pediatrics 1998; 102:68

9. Guyatt GH, Juniper EF, Griffith LE, et al. Children and adult perceptions of childhood asthma. Pediatrics 1997; 99:165–168

10. Mendoza FS. The health of Latino children in the United States. Future Child: Crit Health Issues Child Youth 1994; 4(3):43–72

11. Crain EF, Weiss KB, Bijur PE, Hersh M, Westbrook L, Stein RE. An estimate of the prevalence of asthma and wheezing among inner-city children. Pediatrics 1994; 94:356–362

12. Beckett WS, Belanger K, Gent JF, Holford TR, Leaderer BP. Asthma among Puerto Rican Hispanics: a multi-ethnic comparison study of risk factors. Am J Respir Crit Care Med 1996; 154:894–899

13. The International Study of Asthma and Allergies in Childhood Steering Committee. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema. Lancet 1998; 351:1225–1232

14. Wood PR, Hidalgo HA, Prihoda TJ, Kromer ME. Hispanic children with asthma: morbidity. Pediatrics 1993; 91:62–69

15. Kattan M, Mitchell H, Crain E, Evans R, Islam S. Is There a Difference in Asthma Morbidity Between Latino and African American children? Presented at the meeting of the American Thoracic Society, May 1996, New Orleans, Louisiana, USA

16. National Heart, Lung, and Blood Institute. Highlights of the Expert Panel Report II: Guidelines for the Diagnosis and Management of Asthma. US Department of Health and Human Services, 1997. Available at: http:\\www.nhlbi.nih.gov\nhlbi\lung\asthma\prof\asthgdln.htm

17. Burrows B, Martinez FD, Halonen M, et al. Association of asthma with serum IgE levels and skin-test reactivity to allergens. N Engl J Med 1989; 320:271–277

18. Morgan WJ, Martinez FD. Risk factors for developing wheezing and asthma in childhood. Pediatr Clin North Am 1992; 39:1185–1203

19. Martinez FD, Holberg CJ, Halonen M, et al. Evidence for Mendelian inheretance of serum IgE levels in Hispanic and non-Hispanic white families. Am J Hum Genetics 1994; 55:555–565

20. Martinez FD, Wright AL, Taussig LM, et al. Asthma and wheezing in the first six years of life. N Engl J Med 1995; 332:133–138

21. Colp C, Pappas J, Moran D, Lieberman J. Variants of alpha 1-antitrypsin in Puerto Rican children with asthma. Chest 1993; 103:812–815

22. Colp C, Talavera W, Goldman D, et al. Profile of bronchospastic disease in Puerto Rican patients in New York City: a possible relationship to alpha 1-antitrypsin variants. Arch Intern Med 1990; 150:2349–2354

23. Hsu KHK, Jenkins DE, Hsi BP, et al. Ventilatory functions of normal children and young adults—Mexican-American, white, and black, I: Spirometry. J Pediatr 1979; 95:14–23

24. Dodge R. A comparison of the respiratory health of Mexican-American and non-Mexican-American white children. Chest 1983; 84:587–592

25. Oliveti JF, Kercsmar CM, Redline S. Pre- and perinatal risk factors for asthma in inner-city African-American children. Am J Epidemiol 1996; 143:570–577

26. Fuentes-Afflick E, Lurie P. Low birth weight and Latino ethnicity: examining the epidemiologic paradox. Arch Pediatr Adolesc Med 1997; 7:665–674

27. Call RS, Smith TF, Morris E. Risk factors for asthma in inner-city children. J Pediatr 1992; 121:862–866

28. Rosentreich DL, Eggleston P, Kattan M, et al. The role of cockroach allergy and exposure to cockroach allergen in causing morbidity among inner-city children with asthma. N Engl J Med 1997; 336:1356–1363

29. Richards W. Hospitalizations of children with status asthmaticus: a review. Pediatrics 1989; 84:111–117

30. Whittemore AS, Korn EL. Asthma and air pollution in the Los Angeles area. Am J Public Health 1980; 70:687–696

31. Romieu I, Menesses F, Sienra-Monge JJ, et al. Effects of urban air pollutants on emergency visits for childhood asthma in Mexico City. Am J Epidemiol 1995; 141:546–553

32. McMichael AJ, Anderson HR, Brunekreff B, Cohen AJ. Inappropriate use of daily mortality analyses to estimate longer-term mortality effects of air pollution. Intl J Epidemiol 1998; 27:450–453

33. Martinez FD, Antognoni G, Macri F, et al. Parental smoking enhances bronchial responsiveness in nine-year-old children. Am Rev Respir Dis 1988; 138:518–523

34. Soyseth V, Knogerud J, Boe J. Postnatal maternal smoking increases the prevalence of asthma but not of bronchial hyperresponsiveness or atopy in their children. Chest 1995; 107:389–394

35. Pletsch PK. Environmental tobacco smoke exposure among Hispanic women of reproductive age. Public Health Nurs 1994; 11:229–235

36. Pletsch PK. Prevalence of cigarette smoking in Hispanic women of childbearing age. Nurs Res 1991; 40:103–106

37. Scrimshaw SCM, Iverson E. Health Care Experiences with Epilepsy and Asthma in Los Angeles: A Comparison of Latino Migrants and Latino and Anglo Residents. Presented at the annual meeting of the Society for Applied Anthropology, San Diego, Calif, March 17, 1983

38. Guarnaccia PJ, Pelto PJ, Schensul SL. Family health culture, ethnicity, and asthma: coping with illness. Med Anthropol 1985; 9:203–224

39. Pachter LM, Cloutier MM, Bernstein BA. Ethnomedical (folk) remedies for childhood asthma in a mainland Puerto Rican community. Arch Pediatr Adolesc Med 1995; 149:982–988

40. Matus I, Bush D. Asthma attack frequency in a pediatric population. Psychosom Med 1979; 421:629–636

41. Anderson HR, Bailey PA, Cooper JS, Palmer JC. Influence of morbidity, illness label, and social, family and health service factors on drug treatment of childhood asthma. Lancet 1981; 2:1030–1032

42. Clark NM, Levison MJ, Evans D, et al. Communication within low income families and the management of asthma. Patient Education Counseling 1990; 15:191–210

43. Mrazek DA. Psychiatric Complications of Pediatric Asthma. Ann Allergy 1992; 69:285–290

44. Boxer GH, Carson J, Miller BD. Neglect contributing to tertiary hospitalization in childhood asthma. Child Abuse Negl 1988; 12:491–501

45. Strunk RC, Mrazek DA, Wolfson-Fuhrmann GS, LaBrecque JF. Physiologic and psychological characteristics associated with deaths due to asthma in childhood. JAMA 1985; 254:1193–1198

46. Rodriguez MA, Brindis CD. Violence and Latino youth: prevention and methodological issues. Public Health Rep 1995; 110:260–267

47. Bussing R, Halfon N, Benjamin B, Wells KB. Prevalence of behavior problems in US children with asthma. Arch Pediatr Adolesc Med 1995; 149:565–572

48. Senturia YD, Evans R. Managing asthma in the inner-city: non-medical problems create obstacles to care. Arch Pediatr Adolesc Med 1996; 15(suppl):55

49. Andersen RM. Revisiting the behavioral model and access to medical care: does it matter? J Health Soc Behav 1995; 36:1–10

50. Lara M, Allen F, Lange L. Physician perceptions of barriers to care for inner-city Latino children with asthma. J Health Care Poor Underserved 1999; 10: 27–44

51. Donabedian, A. The definition of quality and approaches to its assessment. In Griffith JR (Ed): Explorations in Quality Assessment and Monitoring. Vol 1. Ann Arbor, Mich, Health Administration Press, 1980,

52. Valdez RB, Morgenstern H, Brown ER, et al. Insuring Latinos against the cost of illness. JAMA 1993; 269: 889–894

53. Pachter LM, Weller SC. Acculturation and compliance with medical therapy. Dev Behav Pediatr 1993; 14:163–168

54. Solis JM, Marks G, Garcia M, Shelton D. Acculturation, access to care, and use of preventive services by Hispanics: findings from HHANES 1982-1984. Am J Public Health 1990; 80(suppl):11–19

55. Finkelstein JA, Brown RW, Schneider LC, et al. Quality of care for preschool children with asthma: the role of social factors and practice setting. Pediatrics 1995; 95:389–394

56. Mitchell H, Lynn H, Crain E, Kercsmar C, Weiss K. An index of access to care for inner-city children with asthma [abstract]. Pediatr Res 1996; 39(suppl 4, pt 2):109A

57. Crain EF, Weiss KB, Kercsmar C, Mitchell H, Lynn H. Access to health care for inner-city children with asthma. Arch Pediatr Adolesc Med 1996; 150(suppl):20

58. Kaufman JS, Cooper RS, McGee DL. Socioeconomic status and health in blacks and whites: the problem of residual confounding and the resiliency of race. Epidemiology 1997; 8:621–628

59. Morgenstern H. Defining and explaining race effects. Epidemiology 1997; 8:609–611

60. Halfon N, Newacheck PW. Childhood asthma and poverty: differential impacts and utilization of health services. Pediatrics 1993; 91:56–61

61. Winsberg M. Specific Hispanics. Am Demogr 1994, Vol 2

62. Wissow LS, Warshow M, Box J, Baker D. Case management and quality assurance to improve care of inner-city children with asthma. Am J Dis Child 1988; 142:748–752

63. Lewis MA, Rachelefsky G, Lewis CE, Leake B, Richards W. The termination of a randomized clinical trial for poor Hispanic children. Arch Pediatr Adolesc Med 1994; 148:364–367

Articles

Latino Children's Health and the Family–Community Health Promotion Model

FERNANDO S. MENDOZA, MD, MPH, *Palo Alto, California; and* ELENA FUENTES-AFFLICK, MD, MPH, *San Francisco, California*

A majority of Latino children in the US live in poverty. However, unlike other poor children, Latino children do not seem to have a consistent association between poverty and poor health. Instead, many poor Latino children have unexpectedly good health outcomes. This has been labeled an epidemiologic paradox. This paper proposes a new model of health, the family–community health promotion model, to account for this paradox. The family–community health promotion model emphasizes the family–community milieu of the child, in contrast to traditional models of health. In addition, the family–community model expands the outcome measures from physical health to functional health status, and underscores the contribution of cultural factors to functional health outcomes. In this paper, we applied the family–community health promotion model to four health coutcomes: low birthweight, infant mortality, chronic and acute illness, and perceived health status. The implications of this model for research and policy are discussed.

(Mendoza FS, Fuentes-Afflick E. Latino children's health and the family–community health promotion model. West J Med 1999; 170:85–92)

In the 21st century medical breakthroughs will improve the health of children, especially those with chronic and disabling conditions. These advancements, however, may not affect all areas of children's health nor all children. While we are on the verge of implanting genes into the cells of children with cystic fibrosis, thereby dramatically changing their lives, we have made far less progress in providing quality health care to poor children with chronic illness, such as asthma, or in decreasing disability and death from accidents and violence. This discrepancy arises in part because socio-environmental factors do not usually respond to "silver bullets." They require, instead, complicated interventions over a sustained period of time to effect resolution. The number of children with health problems that respond to silver bullets, unfortunately, is small, while the large number of those affected by the detrimental effects of poverty continues to grow.

It is clear that along with new technology, the coming century will present child-health researchers and professionals with three challenges. The first will be to increase our understanding of the socioenvironmental factors influencing children's health. The second will be to develop effective, economically feasible health interventions that will have long-term effects on these socioenvironmental factors. The third, and perhaps most important challenge, will be to ensure that all children benefit from these health interventions, particularly those groups of children disproportionately affected by poverty.

In order to meet these challenges, we must understand the multiple factors that affect children's health. Biomedical research has increased our understanding of the effects of physiological disorders and environmental pathogens on biological processes within the human body. The relationship, however, between socioenvironmental factors and health remains poorly understood. Poverty is an important risk factor for poor health, and children living in poverty tend to have poorer health than those not living in poverty.[1–5] For example, Starfield found that poor children have a rate of morbidity from chronic and disabling conditions two to three times that of nonpoor children.[1] Because children living in poverty in the United States have a disproportionate, demographic tendency to be minorities, these children tend to have a worse health status than middle-class white children.[6–9] Newacheck and colleagues, however, reported that the poorer health status of minority children results from their having less access to quality health care, and that this effect is independent of their socioeconomic status.[9] Thus, race and ethnicity are also important covariants in the

From the Department of Pediatrics, Stanford University School of Medicine, Palo Alto, California (Dr Mendoza); Department of Pediatrics, University of California, San Francisco, California (Dr Fuentes-Afflick).

Reprint requests to Dr Fernando S. Mendoza, Division of General Pediatrics, Department of Pediatrics, Stanford University School of Medicine, 750 Welch Road, Suite 325, Palo Alto, CA 94304.

relationship between poverty and health. Yet, not all poor minority children have poor health status; some have unexpectedly high health outcomes in certain areas. Poor Latino children in particular have shown better than anticipated health results, especially in the areas of low birth weight and infant mortality.[10] This disparity in the traditionally observed relationship between poverty and poor health has been termed an epidemiological paradox, in that certain poor children seem to be protected from some of the negative effects of poverty. Some aspect of the socioenvironmental milieu, it seems, may serve as a buffer against the damaging health effects of poverty, and, consequently, give these children a better health profile than one would expect.

In an effort to explain the epidemiological paradox, this paper proposes an alternative model of risk factors for adverse health outcomes. Our "family–community health promotion model" offers a new, conceptual approach to understanding the unexpectedly low rates of adverse health outcomes among some groups of poor children. We examined the usefulness of this model in explaining the current data on the prevalence of low birth weight, infant mortality, chronic illness, and perceived health status in Latino children. None of these health measures follows the traditional relationship between poverty and poor health, and therefore, each provides us with an opportunity to expand our thinking on the subject.

Traditional Model of Health

A general overview of the basic components of health models will put this new model into context. Although various models of health have been proposed in the past, the most basic models of health usually encompass three predictive variables: genetic potential for disease in the individual or population; environmental health risks, such as toxins, infectious agents, malnutrition, or stress; and high-risk behaviors, such as smoking, substance abuse, or early sexual activity, on the part of the individual or populations (Figure 1).[4] Genetic potential is key to the model. At present, we know that a child's genetic potential can determine a variety of risks for poor health, such as a chronic illness, reaction to infectious agents, or the probability of some types of mental illness. Whether this potential is expressed may be influenced by environmental factors, like stress or exposure to infectious agents, and high-risk behaviors, like smoking and improper diet. Thus, the traditional health model postulates that the interactions between an individual's genetic potential for illness or health, and his or her behavioral and environmental risks are important determinants of his or her health status. If the model were extended to a population of individuals, each of these factors would have greater variability due to the multiplicity of individuals, but similar relationships would be anticipated.

In most health models, socioeconomic status, or poverty, affects health status through environmental or behavioral factors. The supposition is that families living in poverty or near-poverty may not have the economic, social, or communal resources needed to keep children in good health. Brooks-Gunn and Duncan suggest that poverty affects children's well-being by influencing health and nutrition, home environment, parental interactions with children, parental mental health, and neighborhood conditions.[5] The deficits associated with poverty may lead to inadequate diets, resulting in poor growth; inadequate housing and increased risk of exposure to lead and other toxins; overcrowding and increased risk for infectious diseases; and community violence that threatens the well-being and, often, the lives of children. Furthermore, the combined effects of these stressors may lead to hopelessness and depression among family members, possibly resulting in high-risk health behaviors and unfavorable familial or parental interactions. Overall, socioeconomic status is the primary determinant of the environmental risks in most health models and is strongly associated with high-risk health behaviors. Consequently, if poverty is part of the individual's environment, its interaction with the genetic–behavior axis will more likely result in a poor health outcome.

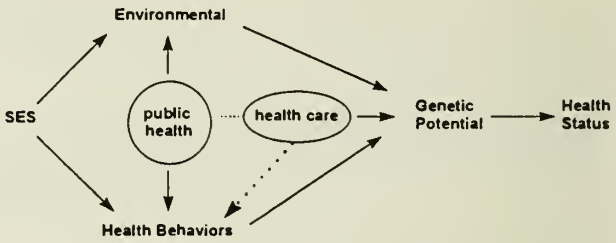


Figure 1.—Traditional health model.

Many health models also include the intervention domains of the medical and public health systems, which mediate health outcomes. The medical care system interacts with the individual patient and, occasionally, with his or her family. In contrast, the public health system interacts with the community as a whole, and occasionally with families, but less often with individuals. The distinct identities of the medical and public health care systems and the economic characteristics of each—one is privately, the other publicly managed—limit their interaction and collaboration. Therefore, it is not unusual that most health models only present the perspective of one or the other. Yet, each system plays an important role in supporting the health of the individual and the population.

The outcomes assessed in most health models generally focus on morbidity and mortality from illness or injury. Health models traditionally use morbidity rates to examine the health status of children, although they occasionally look at mortality rates. While physical examination provides most measures of morbidity, some measures attempt to address more functional morbidities, such as the ability to attend school or participate in routine play. The medical care system, however, focuses primarily on physical health, and, therefore, medically derived morbidities are more commonly measured. For example, the presence or absence of disease and the frequency of health care use are commonly used as morbidity assessments, while the

TABLE 1.—*Socio-Demographic Profiles of Latino Families and Children (Current Population Reports, 1994)*

Group	Percentage of Families in Poverty	Percentage of Children in Poverty	Percentage of Families Headed by a Female	Percentage of Population with High School Education	Percentage of Families without Health Insurance*
Non-Latino white	7.6	13.6	13.0	84.9	11.7
Latino	27.3	40.7	25.7	46.7	—
Mexican American	27.6	40.5	20.3	42.5	38.1
Mainland Puerto Rican	35.4	54.3	43.5	59.4	16.2
Cuban American	17.2	27.0	24.4	64.1	23.9
Central/South American	23.9	35.4	27.3	62.4	—

*Trevio et al.[11]

function of the individual in his or her environment is, unfortunately, less commonly used. This type of assessment, however, an assessment of functional health, is the final, common pathway towards understanding "healthiness," a concept congruent with the World Health Organization's definition of health. If a model of health principally uses medical morbidities, the effects of mediating variables, such as family, social networks, communal resources, and sociocultural traditions, will be infrequently assessed. In contrast, public health models commonly include these medicosocial variables; their results, however, are more population-based and less individual-specific. Is there a way to combine both the medical and public-health perspective in one model of health? The family–community health promotion model expands the environment-behavior axis and extends the measures of health outcomes to encompass this broader view of health and its determinants.

The Family–Community Health Promotion Model

Recent data concerning the health status of Mexican American children reveal the limitations inherent to existing health models. Table 1 shows the demographic profiles of Latino and non-Latino white children. Mexican American children have higher levels of poverty, lower levels of parental education, and limited access to health care than non-Latino white children,[11,12] but, as we will later show, Mexican American children have both unexpectedly low rates of adverse perinatal results and prevalences of chronic and disabling conditions that appear to be unaffected by their level of poverty. This has been termed the epidemiological paradox.

In order to define the factors associated with optimal health outcomes in Latinos, we propose a new health model, the family–community health promotion model (Figure 2). This model retains the three core predictive variables (genetic potential, environmental factors, and health behaviors), but adds several new ones. The family–community health promotion model differs from traditional models, first, by emphasizing the family–community complex, as opposed to the genetic-behavioral-environmental triad. The model stresses specifically the capacity of the family to support the optimum health behaviors of its members, particularly its children, as well as the ability of the family's community to support it in this endeavor. A supposition of the model is that if a family promotes beneficial health behaviors among its members, these lessons will likely be part of the family's culture or tradition. That is to say, these behaviors are apt to be part of the family's identity and history. While family history is a dynamic process, certain aspects of family culture are passed down from one generation to the next. These may include the ways parents nurture their children, the use of extended family members for social support during stressful times, the family's dietary preferences, and other cherished, core family values. These are the sociocultural reference points for good and bad health behaviors and the social norms that support or deter good health.

While the family–community model still predicts that the interactions between the individual's genetic potential for disease, his health behaviors, and his environmental conditions affect health status, it differs from traditional models, secondly, by restructuring health status into two major components, physical and psychological health. These two components contribute to the individual's overall ability to function in day-to-day living; that is, they determine the individual's functional health status. Functional health measures the individual's physical and mental abilities to perform age-appropriate activities. This is a much more robust health measure than commonly used, static measures of morbidity. Moreover, the model predicts that functional health, tempered by the individual's family–cultural milieu through psychological well-being, influences the individual's perception of his health. Therefore, a person's perception of his health status is determined primarily by how he functions in his normal activities, which, in turn, is colored by his cultural perception of "healthy functioning." Thus, one would expect Latinos' health perception to be culturally modified. Indeed, as we will note below, Latino children and their mothers are more likely to have a different view of their health than physicians.

If Latinos believe that their health is poor, they are likely to take some sort of action. This will depend on their access to health care and their perception of what is needed—more nurturing of children, support from family, folk remedies—for resolution of the health problem. Furthermore, the model implies that changes in health perception create a

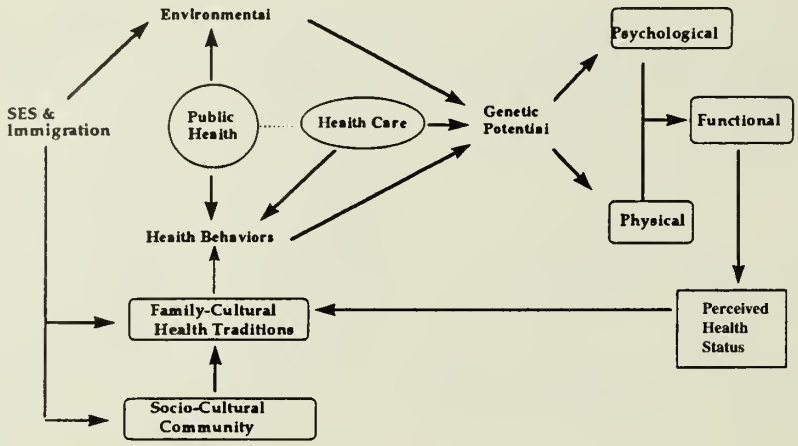


Figure 2.—Family–community health promotion model.

feedback loop to individual and familial health practices. If changes in health behaviors make the individual "feel" better, then the individual is likely to repeat these changes for the same or similar symptoms. These changes may, in this manner, become part of the family's response to a particular set of symptoms. If the response is very successful and, thereby, used routinely, it may become part of the family's culture, like hot liquids for colds, teas for diarrhea, or religious counseling for stressful events. While these responses are most often developed for common self-limited illnesses, they nonetheless provide the basis for responses to more serious, chronic or disabling conditions.

In this model, environmental risk is determined primarily by socioeconomic status, and by the presence or absence of poverty in particular. In addition, it includes immigration status as a determinant of environmental risk to account for the added burden immigrants bear in work and living environments incomparable to those of other poor individuals. For example, although some poor families may live in environmentally hazardous areas, immigrants may be forced, due to lower levels of social integration, to live in environments with greater risk for exposure to harmful toxins like pesticides and lead. This is clearly the case for farm workers, who are predominantly new immigrants, but even in urban areas, immigrants who are poor may need to take more risks in order to survive. It is not unusual for immigrant children and their families to live in crowded conditions—multiple families sharing one house are not uncommon—or to live and play in high-risk, violent areas. Furthermore, because of their immigrant status, whether documented or undocumented, the "safety net" for the poor may be less, if at all, available for immigrants and their children. Yet, for all their increased risk, immigrant families have their cultural milieu that appears to help them and the community ward off poor health.

The following three areas of health have been studied among Mexican American children and found paradoxical according to the traditional model. Each area of study emphasizes a different part of the model as its point of primary focus. Low birth weight and infant mortality are related to the family's cultural norms regarding pregnancy, maternal behaviors, and the perinatal environment. Chronic and disabling medical conditions are used to examine the genetic prevalence of these among Mexican American children and the environmental influence of poverty. Finally, perceived health status is used to examine the disparity between Latino families and physicians with respect to what each considers good health.

Low Birth Weight, Infant Mortality and Latinos

When the result of prematurity or poor growth (the child is small for its gestational age), low birth weight is associated with disabling health and developmental conditions.[13] While recent advances in neonatal medical care have significantly decreased these negative effects, low birth weight still poses a major risk to children's health and development. Both the prevalence of low birth weight and limited access to health care are strongly associated with poverty. Presumably because of their higher poverty rates and lower use of prenatal care, African Americans in the United States have a higher rate of low birth weight infants than non-Latino whites.[14,15] If the same model of health is applied to Latina women, they, too, should have a high prevalence of low birth weight infants owing to their high poverty rate and low use of prenatal care. In fact, Latina women have the lowest use rate of prenatal health services than any other group of women in the United States.[16] Yet, the rate of low birth weight infants among Latina women is only slightly higher than that among non-Latina white women.[17] The relationship between Latino ethnicity and low birth weight infants, however, varies by Latino subgroup. Infants of Latina women of Central or South American, Cuban, and Mexican origin have similar rates of low birth weight, and these rates are similar to the rates among non-Latina white women.[16,17] In contrast, infants of Latina women of Puerto Rican origin have a higher incidence of low birth weight compared to other Latina women and non-Latina white women. Thus, socioeconomic status alone does not

TABLE 2.—*Prevalence of Chronic Medical Conditions (CMC) by Sex, Age, Poverty, and Language Usage (Percentage with CMC)**

	Mexican American	Mainland Puerta Rican	Cuban American
Total Group	3.9	6.2	2.5†
Sex			
Male	3.9	6.2‡	2.1†
Female	4.0	6.3‡	2.9†
Age			
0–5 y	2.3‡,§	7.4‡	0†
6–11 y	4.5	6.8‡	5.3†
12–18 y	4.9	5.1‡	1.8†
Poverty Status			
Poor	3.7‡	6.8‡	1.7†
Not Poor	4.1	5.4‡	2.8†
Home Language: 6m–11y			
Spanish	3.8‡	7.2†	1.0†
English	3.2‡	7.8‡	8.3†
Both	4.3†	3.9†	5.0†
Lang. Preference: 12–18y			
Spanish	1.8†	0†	0†
English	5.2†	2.6†	3.0†
Both	3.7†	6.4†	0†

*Percentages calculated from sample weights.
†Population estimate is unreliable, and therefore, estimate only reflects attributes of examined subjects.
‡Population estimate does not meet usual reliability standards and can only be used for an approximation of the true population estimates.
§Chi-square adjusted for sample weights and design effect $P < .05$
Source: Mendoza et al.[17]

determine the seemingly complex relationship between ethnicity and low birth weight.

The relationship between behavioral, medical, obstetrical, and health-service factors does not consistently predict rates of low birth weight among Latina women.[15] While younger maternal age is associated with an increased risk of low birth weight in the general population, it is not consistently linked to low birth weight among Latina women.[15] Similarly, lack of prenatal care has not been consistently associated with increased low birth weight among Latina women, although prenatal care is an important component of the public-policy interventions aimed towards reducing the incidence of other adverse birth outcomes.[17–19] Thus, traditional risk factors do not predict low-birth-weight infants among Latinos reliably, which suggests that other factors may be involved, factors such as sociocultural and nutritional influences.[20–25] Guendelman has reported that Mexican American women report lower consumption of tobacco, alcohol, and caffeine.[25] Others have reported similar findings and noted that these risk factors increase with acculturation.[21–24] This suggests that nonacculturated women have better than expected perinatal outcomes resulting from their health habits surrounding pregnancy, habits which their families, communities, and culture appear to support.

A similar picture emerges when considering infant mortality.[26] While this is not a measure of chronic illness or disability, it is worthwhile noting that the factors associated with low birth weight are also associated with infant mortality. Thus, interestingly, infant mortality, like low birth weight, is lower than expected among Latinos, particularly new immigrants.[26] In fact, despite high levels of poverty and low access to health care, infants born to Mexican immigrants have an infant mortality rate similar to that of non-Latino white, middle-class infants. Therefore, incidences of low birth weight and infant mortality in Latino children are significantly lower than would be predicted by a traditional model of health. According to the family–community health promotion model, a positive cultural milieu surrounding the issue of pregnancy and child-rearing would explain this discrepancy, and current data supports this conclusion.

The Prevalence of Chronic and Disabling Conditions Among Latino Children and Adolescents

The medical community has very little data on the prevalence of chronic and disabling conditions among Latino children and adolescents. The Hispanic Health and Nutrition Examination Survey (HHANES), conducted by the National Center for Health Statistics from 1982 to1984, provided the first physician-assessed prevalences of chronic medical conditions among Mexican American, mainland Puerto Rican, and Cuban American children and adolescents.[17] These findings showed that Mexican Americans and Cuban Americans had three to five percent prevalence of chronic medical conditions, as did other US children. In contrast, six percent of mainland Puerto Rican children and adolescents had chronic medical conditions (Table 2). The higher rate among Puerto Ricans resulted almost entirely from a higher rate of chronic respiratory problems, principally asthma. The prevalences of chronic medical conditions among all groups surveyed did not vary by sex, age (except for Mexican Americans), socioeconomic status, or level of acculturation, as measured by language usage (Table 2). This finding is consistent with the hypothesis assumption that for the most part genetic, rather than socioeconomic factors determine chronic illness, and that rates of chronic illness increase with age, as is seen among Mexican American children. Therefore, it appears that the prevalence of chronic medical conditions among Latino children resembles that of other US children, with the exception of asthma in Puerto Rican children. This exception suggests that Puerto Rican children may have a greater, genetic predisposition for asthma.

The HHANES also supplied information provided by respondents who reported both present and prior medical and developmental conditions (Table 3).[27,28] These data showed that Mexican American mothers reported rates similar to or lower than US norms for asthma, coordination problems, psychological and behavioral problems, speech problems, and mental retardation. In contrast, mainland Puerto Rican mothers reported higher rates of some medical and developmental conditions than

TABLE 3.—*Reported Medical Conditions of Mexican American and Mainland Puerto Rican Children Aged 5–11 Years from HHANES*

	Mexican American				Mainland Puerto Rican			
	Percentage with Condition		Percentage of Children		Percentage with Condition		Percentage of Children	
Condition	Ever	Now	Treatment	Treated	Ever	Now	Treatment	Treated
Anemia	7.9	1.0	92	93	16.0	2.7	92	96
Asthma	4.9	3.1	100	93	22.0	11.5	100	98
Other lung diseases	3.8	0.8	100	98	3.0	1.0	100	98
Heart conditions	3.6	1.9	91	90	7.3	5.0	51	100
Urinary tract infections	6.0	1.3	89	98	3.3	0.6	100	100
Seizures	3.4	0.6	88	98	5.3	1.3	85	96
Poisons	1.2	0	0	100	1.9	0	0	100
Coordination problems	1.2	1.0	69	100	2.3	1.5	74	100
Psychological behavioral	1.5	1.3	37	66	5.9	5.7	74	100
Speech problems	4.2	3.5	46	40	8.6	6.7	70	81
Mental retardation	0.5	0.5	100	—	3.1	3.1	88	—

HHANES = Hispanic Health and Nutrition Examination Survey

Source: Mendoza et al.[27,28]

Mexican American mothers. According to the reports of Puerto Rican mothers, 11.5% of their children have asthma, 5.7% have psychological and behavioral problems, 6.7% have speech problems, and 3.1% have mental retardation. Overall, Puerto Rican mothers reported greater numbers of children with medical and developmental conditions. We do not know if this data indicates an actual, increased prevalence of these conditions, or if it reflects greater knowledge on the part of these mothers about their children's conditions, thus greater access to care. This question requires further research.

Mothers also reported whether their children had obtained treatment for their conditions. In general, treatment for physical disease was obtained, while treatment for behavioral, developmental, and psychological conditions was less frequently obtained, particularly for Mexican American children.[27,28] Compared to other groups of children, Mexican American children have less access to health care as a result of limited health insurance coverage.[10–12] In contrast, mainland Puerto Rican children have higher rates of insurance coverage because of their citizenship status. Yet, when we examine the health of Puerto Rican children, it seems that they have higher rates of chronic and disabling conditions than either Mexican American or Cuban American children. Although Mexican American children come from families that have high poverty rates and low levels of education, they appear, from our current, limited information, to do better than expected in their health, and better compared to Puerto Rican children. At present this is documented by a lower prevalence of low birth weight, and chronic medical and developmental conditions. It remains to be seen whether these findings will persist after controls for reporting biases are examined, and further research will be required to determine what factors lead to different outcomes among Latino subgroups.

A cautionary note, however, must be given. If one examines the rates of acute illnesses, particularly of infectious diseases, all Latino children seem to fare less well. Latino children have higher rates of tuberculosis, measles, and parasites than other US children.[29] Furthermore, limited health care access has resulted in low immunization rates, thus to higher frequencies of childhood illness.[10,29] Other acute illnesses, such as gastroenteritis and pneumonia, are common among Mexican American children because of their environment and frequently go untreated because of lack of health care access.[29] Such children are not uncommonly hospitalized for complications resulting from these acute illnesses. The combination of acute illness and lack of health care may result in significant morbidity, causing disabling conditions for Latino children. Likewise, Latino children suffer from high rates of accidents and violence.[30] These conditions, if not appropriately treated or prevented, can also have long-term chronic effects on these children. With a more restrictive health care system, newer surveys may find changes in the prevalences of chronic medical conditions among Latino children.

Thus, the family–community health promotion model predicts that chronic and disabling medical conditions develop out of the interaction between genetic potential and environmental and behavioral risks. Chronic medical conditions that arise primarily from a genetic predisposition, like asthma, are less affected by poverty, while those disabilities that result from exposure to environmental pathogens are clearly more common among the poor. In either case, lack of access to health care is a major, mediating factor in the health of Latino children. Consequently, although Mexican American children have rates of incidence for certain health conditions similar to those of non-Latino white children, their limited access to care makes them more likely to suffer morbidity from these conditions.

The Perceived Health Status of Latino Children

The HHANES assessed the perception of the child's and adolescent's health from the perspectives of the child (6–11 years), adolescent, mother, and survey physician. Physicians identified only 1% of all children surveyed in HHANES as in fair or poor health, while Mexican American and mainland Puerto Rican mothers identified 15% to 20% of their children and adolescents as in fair or poor health.[27,31] Among children six years of age and older, about 10% to 19% believed they were in fair or poor health, as opposed to 5% to 10% percent of other children in the United States. When mothers' perceptions of their children's health were examined, the data showed no difference by the child's sex or age, but did show a significant difference by their poverty status and home language.[28] Mothers of poor and Spanish-speaking children were more likely to believe their children were in poor health.[27] Children with a chronic medical condition were seen as vulnerable, with 27% and 41% of Mexican American and mainland Puerto Rican children, respectively, being rated in poor health by their mothers.[27] Yet, the physician ratings were significantly lower, at 11.6% and 6.4%, respectively. This discrepancy suggests either that mothers are identifying in their children health problems not easily identified by physicians, or that Latina mothers and their children have a different perception of health, one that is not fully appreciated by traditional measures (physical disease findings). This clear disparity between physicians and Latina mothers and children has far reaching implications for health care use, compliance and patient satisfaction. Examining the functional health-perceived health linkage among Latinos will be essential to better understanding the health care needs of this population and to testing the usefulness of the family–community health promotion model.

Research and Policy Implications

The implications of this model for research and policy are several. First, measures of functional health are needed for Latino and non-Latino groups in order to use the model fully to predict outcomes. As the physicians' assessment of Latino children demonstrated, physical health assessments are limited. It is important to study and understand the social and cultural histories of families and communities if we are going to use their strengths effectively. Moreover, it is essential to understand better how these familial–community assets support children's development. Garcia-Coll has suggested that children from different ethnic groups have culturally-derived, developmental pathways.[32] Studying these pathways would be very important to gaining a better understanding of poor, ethnic children with chronic and disabling conditions. As we examine the effect of environment on these children, we need to identify the various forms of poverty and their influence on children. We should be concerned not only about lead and pesticides, but also about the effects of chronic violence and other stressors. Most importantly, we need to refocus policy toward helping families, rather than treating disease, and we need to see immigrants as a useful and essential resource for this country's future. The family–community health promotion model provides a better conceptual framework for developing and researching hypotheses about Latino children and families than the traditional health model. It also provides a better explanation of the existing epidemiological health paradox. As the United States becomes more ethnically diverse, we will need models of health robust enough to account for the effect of cultural milieu on health. Though this is clearly not a new idea, it is one strongly rooted in public health practices. Our current imbalance in the health care system, however, requires that we focus our attention on the true, major determinants of health for children. We hope that our model will stimulate further discussion.

REFERENCES

1. Starfield B. Childhood morbidity: comparisons, clusters, and trends. Pediatrics 1991; 88:519–526

2. Martorell R, Mendoza FS, Castillo R. Poverty and stature in children in linear growth retardation in less developed countries. In Waterlow JC (Ed), Nestle Nutrition Workshop Series: 14. New York, Nestle Ltd. Vevey/Raven Press, Ltd., 1988, pp 57–73

3. Pollitt E. Poverty and child development: relevance of research in developing countries to the United States. Child Dev 1994; 65:283–295

4. Wise P, Meyers A. Poverty and child health in children at risk. Pediatr Clin North Am 1988; 35:1169–1186

5. Brooks-Gunn J, Duncan G. The effects of poverty on children. Future Child 1997; 7(2):55–71

6. Givens S, Moore M. Status report on maternal and child health indicators. Perinat Neonatal Nurs 1995; 9:8–18

7. Simpson G, Bloom B, Cohen R, Parsons P. Access to Health Care. Part 1: Children. Vital and Health Statistics. Series 10: Data From the National Health Survey, Vol. 196, July 1997, pp 1–46

8. Singh G, Yu S. U.S. childhood mortality, 1950 through 1993: trends and socioeconomic differentials. Am J Public Health 1996; 86:505–512

9. Newacheck P, Hughes D, Stoddard J. Children's access to primary care: differences by race, income, and insurance status. Pediatrics 1996; 9:26–32

10. Mendoza FS. The health of Latino children in the United States. Future Child 1994; 4(3):43–72

11. Trevio F, Moyer M, Valdez R, Stroup-Benham C. Health insurance coverage and utilization of health services by Mexican Americans, mainland Puerto Ricans, and Cuban Americans. JAMA 1993; 269:889–893

12. Halfon N, Wood D, Valdez R, Pereyra M, Duan N. Medicaid enrollment and health services access by Latino children in inner-city Los Angeles. JAMA 1997; 277:636–641

13. Gortmaker S, Sappenfield W. Chronic childhood disorders: prevalence and impact. Pediatr Clin North Am 1984; 31:3–18

14. Kessel SS, Kelinman JC, Koontz AM, Hog CJR, Berendes HW. Racial differences in pregnancy outcomes. Clin Perinatol 1988; 15:745–754

15. Fuentes-Afflick E, Lurie P. Low birth weight and Latino ethnicity: examining the epidemiologic paradox. Archiv Pediatr Adolesc Med 1997; 151:665–74

16. Ventura SJ, Martin JA, Taffel SM, Mathews TJ, Clarke SC. Advance report of final natality statistics, 1993. Monthly Vital Statistics Report 1995; 44(Suppl):1–88.

17. Mendoza FS, Ventura SJ, Valdez RB, et al. Selected measures of health status for Mexican-American, mainland Puerto Rican, and Cuban-American children. JAMA 1991; 265:227–232

18. Balcazar H, Cole G, Hartner J. Mexican Americans' use of prenatal care and its relationship to maternal risk factors and pregnancy outcome. Am J Prev Med 1992; 8:1–7

19. Collins JW, Shay DK. Prevalence of low birth weight among Latino infants with United States-born and foreign-born mothers: The effect of urban poverty. Am J Epidemiol 1994; 139:184–192

20. Dowling PT, Fisher M. Maternal factors and low-birth-weight-infants: A comparison of blacks with Mexican-Americans. J Fam Pract 1987; 25:153–158.

21. Scribner R, Dwyer, JH. Acculturation and low birth weight among Latinos in the Latino HANES. Am J Public Health 1989; 79:1263–1267

22. Guendelman S, English PB. Effect of United States residence on birth outcomes among mexican immigrants: an exploratory study. Am J Epidemiol 1995; 142(9 Suppl):530–538

23. Guendelman S, Gould JB, Hudes M, Eskenzai B. Generational differences in perinatal health among the Mexican-American population: Findings from HHANES, 1982-84. Am J Public Health 1990; 80(Suppl):61–65

24. Guendelman S, Abrams B. Dietary intake among Mexican-American women: Generational differences and a comparison with white non-Latino women. Am J Public Health 1995; 85:20–25

25. Guendelman S, Abrams B. Dietary, alcohol, and tobacco intake among Mexican-American women of childbearing age: results from HANES data. Am J Health Promotion 1994; 8:363–372

26. Becerra J, Hogue C, Atrash, J, Perez N. Infant mortality among Hispanics: a portrait of heterogeneity. JAMA 1991; 265:217–221

27. Mendoza FS, Takata GS, Martorell R. Health status and health care access for mainland Puerto Rican children: results from the Hispanic health and nutrition survey. In Lambert G, Gracia-Coll C (Eds). Puerto Rican Women and Children: Issues in Health, Growth and Development. New York, NY. Plenum Press, 1994 p. 211

28. Mendoza FS, Martorell R, Castillo R. Health and Nutritional Status of Mexican-American Children. Final Report Grant MCJ-060518-02-1, The Maternal and Child Health Research Program, 1989

29. Sumaya, C. Major infectious diseases causing excess morbidity in the Hispanic populations, In Furino A (Ed). Health Policy and the Hispanic. Boulder, Colo, Westview Press, 1992, pp 76–96

30. State of Hispanic Health. Washington, DC, National Coalition of Hispanic Health and Human Services Organizations, 1992

31. Mendoza FS, Ventura SJ, Saldivar L, Baisden K, Martorell R. The health status of U.S. Latino children, In Furino A (Ed). Health Policy and the Hispanic. Boulder, Colo, Westview Press, 1992, pp 76–96

32. Garcia-Coll C. Developmental outcome of minority infants: A process-oriented look into our beginnings. Child Dev 1990; 61:270–289

Articles

Placebo Medication Use in Patient Care: A Survey of Medical Interns

JEFFREY T. BERGER, MD, FACP, *Mineola, New York*

The use of placebo medication, long recognized by clinicians, often has serious practical implications, such as patient deception. Past evidence has suggested that resident physicians tend to misuse placebo medication. Interns from two consecutive years of a residency program were surveyed anonymously to assess their knowledge and use of placebos. Of the 74 interns surveyed, 44 (59%) were familiar with placebo use in patient care. Fifty percent of these interns familiar with placebo use had learned about placebos from another physician. All interns who had learned about placebos during their internships had learned from another physician, whereas interns who had gained their knowledge of placebos as medical students were as likely to have learned from the medical literature as they were to have learned from a physician ($P = 0.027$). Interns aware of placebo use were more likely to consider placebo administration for suspected, factitious pain ($P = 0.022$). The present study uncovered no relationship between interns' estimations of placebo efficacy and the utility they attributed to placebos in assessing a complaint of pain. This suggests that conceptual inconsistencies underlie their use of placebos. Interns often learn of placebos as medical students and are influenced by physician-mentors. Placebo use in patient care is an area of attention for medical educators.

(Berger JT. Placebo medication use in patient care: a survey of medical interns. West J Med 1999; 170:93–96)

With reported response rates of 30% to 50%, placebo medication and its effects have been long recognized in medicine.[1] Physicians widely accept placebo use in patient care.[2–5] They consider its use when they suspect factitious pain or non-somatic suffering, or wish to limit a patient's exposure to narcotic analgesics. Placebo use, however, frequently involves patient deception. This deception runs contrary to accepted notions of patient autonomy and informed consent to treatment,[6–8] and a patient's trust may be harmed should he or she discover the deception.[9] Furthermore, physicians' orders for placebos may compromise the ethical integrity of other health care professionals, such as nurses, who often administer the placebo.

A prior study[4] that assessed resident physicians' attitudes toward placebos concluded that these physicians underestimate placebo efficacy and tend to misinterpret a response to placebo as evidence of nonorganic pain. We have little additional, empirical information about house staff use of placebos. This survey was designed to assess medical interns' understanding and use of placebos.

Methods

The survey consisted of ten open- and closed-ended questions. A placebo was defined as an inactive substance administered to a patient in place of a medication. Interns were asked about their familiarity with placebo use in patient care. Interns aware of this practice were asked to state when in their training, and from whom, they had learned of placebo use. They were asked to indicate the number of orders for placebos they had written during internship, to identify the placebo medication, and to indicate the number of placebos they had administered directly. Interns were also asked to relate any disagreements with their decision to use a placebo and whether the recipient was aware of its use. All interns were asked to estimate general rates of response to placebo and to describe their understanding of the utility of placebo administration in differentiating organic pain from non-organic pain. They were also asked to describe situations in which they would most likely consider using a placebo. Survey responses were studied using chi-square analysis and paired *t*-tests.

Surveys were distributed seven weeks prior to the end of the internship and collected within four weeks of distribution. Interns were surveyed anonymously, and completion was voluntary. There was no penalty for noncompliance, although telephone reminders encouraged participation.

From the Department of Medicine, Winthrop-University Hospital, Mineola, New York.
Reprint requests to Jeffrey T. Berger, MD, FACP, Winthrop-University Hospital, 222 Station Plaza North, Suite 518, Mineola, NY 11501.

Subjects

Subjects were interns from two consecutive years of an internal medicine residency program at a 485-bed university-affiliated community hospital. The survey included interns from the preliminary program (n = 59) and categorical program (n = 30). The two internship-classes represented 28 medical schools. Of the 89 interns eligible for the survey, 74 (83%) responded; however, 13 surveys were returned partially completed. The profiles of the two internship-classes were similar in gender, degree (MD versus DO), and training program (preliminary versus categorical). The two training programs were dissimilar in that 67% of preliminary interns and 35% of categorical interns were male. Of the preliminary interns, 1 in 50 had graduated from a school of osteopathic medicine, whereas 7 in 20 categorical interns had graduated from a like school.

Results

Knowledge of Placebo Use in Patient Care

The survey assessed interns' knowledge of placebo use and the source of this knowledge. Of the 74 interns surveyed, 47 (64%) were aware of the clinical practice of using placebos. Of these 47 interns, 44 (94%) described the source of their knowledge of placebo use. Nine had learned of placebo use from more than one source. Half had learned from another physician, 10 (23%) from another intern, 8 (18%) from a resident physician, 6 (14%) from an attending physician, 2 (4.5%) from nursing staff, and 19 (43%) from reading medical literature. The survey revealed no relationship between familiarity with placebo use and degree, training program, or intern gender.

Of the 47 interns familiar with placebo use, 35 (74%) had learned of the practice as medical students. An additional 7 (15%) learned of the practice during their internships. All interns who had learned of placebo use during internship learned from a physician, whereas interns who had learned as medical students were as likely to have learned from the medical literature as they were to have learned from a physician (P = 0.027).

Use of Placebos

When asked if they had ordered a placebo during their internship, 45 (96%) of the 47 interns aware of placebo use responded. Of that group, 38 (84%) had never ordered a placebo, and 7 (16%) had ordered 1 (n = 4) or 2 (n = 3). Only one intern reported having actually administered a placebo. The survey discovered no relationship between interns who had ordered placebos and their program, gender, or how and when they had learned of placebos. Of the ten placebos ordered during internship, two were reported as tablets, two as intravenous saline, and five as intramuscular saline. Interns reported that none of their patients had been aware of placebo use. In five of the ten reported instances, attending physicians were aware of placebo use and none had objected. In one case, however, a nurse disagreed with an intern's order for a placebo.

Understanding the Placebo Effect

When asked to estimate the efficacy of placebo in pain relief, 70 (95%) of 74 interns responded. Of this group, 25 (36%) interns underestimated and 12 (17%) overestimated the response rate. There was no relationship between the interns' estimation of placebo response and prior familiarity with placebo use, training program, medical degree, gender, or source of knowledge of placebo use.

When asked to describe the utility of placebo administration in differentiating factitious or nonsomatic pain from organic pain, all interns responded, and 50 (68%) believed placebo administration to be a useful test. There was no relationship between interns' judgment concerning the utility of placebo administration and their self-reported awareness of placebo use, training program, medical degree, or gender. Interns previously unaware of placebo use did not differ from those aware of placebos in correctly describing placebos' useless role in assessing a complaint of pain. In no instance did the survey reveal a relationship between an intern's estimation of placebo effect and the utility he or she attributed to placebo administration as a test for factitious pain (chi-square test, P = 0.537).

Circumstances of Use

Of the 74 interns surveyed, 66 (89%) supplied descriptive data regarding the circumstances in which they would most likely consider using a placebo. The responses were categorized as placebos never used and placebos used for direct patient benefit, suspicion of factitious pain, history of substance abuse, psychiatric illness or psychiatric component to the complaint. Of the 66 interns who supplied data, 32 (48%) were likely to use a placebo when they suspected factitious pain. Interns previously aware of placebo use were more likely than those previously unaware to order a placebo for suspected factitious pain (P = 0.022). In addition, 12 (18%) interns said that they would likely prescribe placebos for patients with a history of substance abuse and 11 (17%) said that they would likely prescribe placebos for patients with a history of psychiatric illness or with a suspected psychological component to their complaint. Interns with no prior knowledge of placebo use in patient care appeared more likely to exclude placebo use under any circumstances (P = 0.051), although 2 (3%) of the 66 interns who supplied descriptive data said that they would consider using placebos for patient benefit only when all other options and resources had been exhausted. The survey found no significant relationship between circumstances of likely placebo use and intern gender or program.

Comment

The survey indicates that placebos are used infrequently in the medical service studied, as less than 10% of the interns questioned reported such activity. A striking finding is the poor correlation between interns' estimations of placebo efficacy and their statements about

the usefulness of placebos in assessing pain. This finding suggests that the utility attributed to this use of placebos is inconsistent with interns' recognition of the placebo effect. Interns perceived a patient's response to a placebo as indicative of factitious pain, although a widely-used medical pharmacology text states, "Relief or lack of relief of symptoms upon administration of a placebo is not a reliable basis for determining whether the symptoms have a psychogenic or somatic origin".[10] This survey did not explore the substance of interns' instruction. Such information would assist the development of more explicit material for medical school curricula for use in reinforcing placebo-related concepts. Supervising physicians who accept or tolerate house-officer use of placebos disservice the physician-in-training. Opportunities may be lost both for mentoring house staff in addressing patients' psychological needs and for developing constructive approaches to the "difficult" patient.[11–14]

Interns' knowledge of placebos appears to be influenced by physician-mentoring during medical school studies and internship training. Misinformation may be reinforced by imprecise abstraction in the medical literature, which describes both the power of the placebo and ethical implications of its use. Placebo use is inappropriate as a diagnostic test and unethical when coupled with patient deception. Placebo use may be appropriate when the patient has consented, in advance, to the random integration of placebo medication into his or her pain management regimen. The educators of physicians need to define clearly the appropriate and inappropriate use of placebos.

Although objection to placebo use was rarely reported, the degree of attending physician and nurse concurrence with interns' placebo use is not clear. Most placebos, we assume, were administered by nurses, because only one intern described administering a placebo. An assessment of nursing experience with placebo use would be enlightening.

Of the interns eligible for inclusion in the study, 15 (17%) did not respond. These interns may have avoided participation because they suspect that placebo use is unethical. On the other hand, nonresponders may have been unfamiliar with the subject, thus uninterested in the study. The nonresponders' bias is therefore unclear. The high participation rate of eligible interns, however, limits any effect this bias may have had.

Interns' continued misunderstanding of placebos opens the door for misuse and may place patients at risk for deception and undertreatment. Patients with either "unconvincing" clinical presentations or psychiatric illnesses appear to be most vulnerable. Some patients who are given placebos will immediately benefit through the relief of symptoms without the risk of side effects from medication. If discovered, however, the attendant deception may jeopardize both the patient's trust in health care professionals and his or her future care. Furthermore, routine placebo use by physicians could eventually harm the reputations and integrity of medical professionals. A management alternative more constructive than placebo use is available in virtually all clinical circumstances.

We do have methodological concerns with the study. First, the limited number of participating subjects may have rendered additional trends and subset findings indiscernible. The subgroup of placebo-ordering interns was too small, for instance, to assess group-specific characteristics. Second, surveying two internship classes in sequential years may have introduced a bias in the second class of interns who were supervised by residents who were survey participants during the preceding year. The house staff, however, received no formal placebo-related instruction during the study period. Relying on interns' recollection of events of the past year is, admittedly, fraught with imprecision, but precise mechanisms for tracking placebo use are difficult to develop. Placebos used are commonly saline flushes, for which neither pharmacy nor nursing accounts. Simultaneous surveys of nursing staff might provide some corroboration of the interns' reports. Third, the definition of placebo used for this study may have contributed to under-reporting. This definition, chosen for its simplicity, does not encompass impure placebos, which are active substances that have no problem-related activity. The respondents, however, did not appear to appreciate this distinction. Furthermore, questions of definition should not affect interns' understanding or likely use of placebos.

This study provides important insights into house-staff use of placebos. The data corroborate earlier evidence that interns' perception of the utility of placebos in testing for factitious pain is inconsistent with their understanding of the placebo effect. This knowledge is acquired early in training and is largely mentor-dependent. Placebo use in patient care is an area requiring attention for physicians-in-training and for the educators of medical students and house staff.

Acknowledgments

The author is grateful to Edith Flaster, Winthrop-University Hospital, for her assistance in data analysis and to both Debra Majerovitz, PhD, Memorial Sloan Kettering, and Nancy Foldi, PhD, Winthrop-University Hospital, for their invaluable comments during the preparation of this manuscript.

REFERENCES

1. Beecher HK. The powerful placebo. JAMA 1955; 159:1602–1606

2. Thomson RJ, Buchanan WJ. Placebos and general practice: attitudes to, and use of, the placebo effect. N Z Med J 1982; 95:492–494

3. Gray G, Flynn P. A survey of placebo use in a general hospital. Gen Hosp Psychiatry 1981; 3:199–203

4. Goodwin JS, Goodwin JM, Vogel AV. Knowledge and use of placebos by house officers and nurses. Ann Intern Med 1979; 91:106–110

5. Schwartz RK, Soumerai SB, Avorn J. Physician motivation for nonscientific drug prescribing. Soc Sci Med 1989; 28:577–582

6. Brody H. The lie that heals: the ethics of giving placebos. Ann Intern Med 1982; 97:112–118

7. Kleinman I, Brown P, Librach L. Placebo pain medication: ethical and practical considerations. Arch Fam Med 1994:453–457

8. Bok S. The ethics of giving placebos. Sci Am 1974; 231:17–23

9. Lynoe N, Mattsson B, Sandlund M. The attitudes of patients and physicians towards placebo treatment: a comparative study. Soc Sci Med 1993; 36:767–774

10. Goodman LS, Gilman A, Rall TW, Nies AS, Taylor P. Goodman and Gilman's the Pharmacologic Basis of Therapeutics. New York, NY, Pergamon Press, 1990, p 72

11. McCauley J, Kern DE, Kolodner K, et al. The "battering syndrome": prevalence and clinical characteristics of domestic violence in primary care internal medicine practices. Ann Intern Med 1995; 123:737–746

12. Briggs GW, Replogle WH. Effect of communication skills training on residents' attitudes towards their patients. Acad Med 1991; 66:243

13. Rosenberg M, Commerford K, Driever M. Identification of psycho social distress: a comparison of internal medicine and family medicine residents. J Gen Intern Med 1991:529–534

14. Eisenthal S, Stoeckle JD, Ehrlich CM. Orientation of medical residents to the psycho social aspects of primary care: Influence of training program. Acad Med 1994; 69:48–54

Articles

International Travel and Vaccinations

MOHAMMED KALEEM RIZVON, MBBS; SAMIA QAZI, MBBS;
and LAURIE ANNE WARD, MD; *East Meadow, New York*

With the increase in global travel, no disease is beyond the reach of any population. Traveling patients should be advised to follow food and water precautions and encouraged to receive the recommended immunizations. Travel medicine plays a vital role not only in limiting the morbidity of travel-related illnesses but also in limiting the spread of diseases. This article addresses the common issues related to travel, reviews the care of the immunocompromised traveler, and updates the available vaccinations and prophylactic regimens available to limit sickness abroad.

(Rizvon MK, Qazi S, Ward LA. International travel and vaccinations. West J Med 1999; 170:97–103)

The extent of travel in this day and age is unprecedented. About 2.5 billion people passed through airports in 1996 alone. The greater range of travel is associated with increased risks of diseases and outbreaks in areas not usually associated with the disease.[1] More than two-thirds of cases of typhoid fever in the United States follow foreign travel.[2] More than 30 million people living in industrialized countries travel to regions where hepatitis A is highly endemic, and hence, they are at risk of contracting the disease.[3] Many diseases prevalent in developing countries are food- and water-borne, making them easily transmissible to visitors. Following food and water precautions and getting vaccinations against the common diseases associated with travel, however, can minimize the risks of acquiring travel-related illnesses.

Very few vaccinations, such as the yellow fever vaccination required for travel to many countries in Africa and tropical South America, are *required* for travel. Many traveling patients, however, are unaware of the vaccine *recommendations* for travel and thereby expose themselves to substantial risks by traveling unprotected.

General Advice to Travelers

- Appointments to travel medical centers should be made four to six weeks before travel. Immunocompromised travelers, patients with chronic cardio-respiratory problems, and travelers wishing to relocate to a different country should be seen much earlier to assess the risks associated with travel and receive appropriate vaccinations.
- Carry an updated vaccination certificate, the address and telephone number of your physician in the United States, and, for cardiac patients, a copy of an old EKG with other required travel documents. Prescription medications should be transported in carry-on luggage. In addition, travelers should carry written prescriptions for generic name medications in case additional medications are needed. Keep prescription medications in their original bottles.
- Carry a standard first-aid kit[4] with thermometers, sterile cotton, tweezers, adhesive tapes, bandages, antiseptic solutions, sunscreens with a minimum SPF >15, analgesics, antihistamines, and medications for motion sickness. Dimenhydrinate (Dramamine) and scopolamine are effective medications that can be used prophylactically for motion sickness.
- Prepackaged oral rehydrant solutions can also be carried to treat dehydration associated with diarrhea.
- Follow the recommended food and water precautions.

Medical Assessment of a Traveler

- While waiting to be seen, traveling patients should be asked to complete a questionnaire that includes a detailed medical history, list of all medications with allergies to medications, immunization history, date of last menstrual period, and itinerary with detailed travel plans including outdoor activities.
- Health advice regarding food and water precautions (Table 1), a travel kit, and accessibility of health care abroad are essential. Patients should be advised to clarify their existing coverage with the insurance companies, and if needed, purchase additional insurance including evacuation insurance. This may be especially important for the immunocompromised traveler.

From the Division of General Internal Medicine, Nassau County Medical Center, East Meadow, New York.

Reprint requests to Mohammed Kaleem Rizvon, MBBS, Attending Physician, Division of General Internal Medicine, Nassau County Medical Center, East Meadow, NY 11554 (e-mail: Mrizvon@aol.com).

TABLE 1.—*Food and Water Precautions During Travel*

Food and water precautions
Avoid salads.
Use bottled water at all times.
Avoid eating from street vendors.
Do not add ice cubes to beverages.
Eat fruits with thick skins that can be peeled.
Avoid improperly cooked items such as shellfish.
Preferably use bottled water to brush teeth.

• Patients should be advised how to get medical assistance abroad in case of any emergency (Table 2). United States Consulates and some credit card companies can be of assistance. The International Association for Medical Assistance to Travelers (IAMAT) prints an updated worldwide list of membership doctors and health institutions and is a valuable guide to travelers needing medical assistance overseas.

• Information about vaccine recommendations is now available on the Internet and is easily accessible.[5]

• The final immunization program depends on the traveler's destination, availability of time before departure, length of trip, health status, and planned activities.

• Patients with complex travel plans, pregnant travelers, immunocompromised patients, travelers with history of severe cardiopulmonary disease, and returned travelers with fever or diarrhea should be referred to travel medicine specialists.

Disease and Vaccine Information

Travelers' Diarrhea

Travelers' diarrhea occurs worldwide and is most prevalent in travelers visiting developing countries. It is characterized by the onset of watery diarrhea usually within one week of travel. The most common associated symptoms include abdominal cramping, sometimes followed by bloody stools and vomiting. Fever is unusual and is recorded in 1%–10% of cases.[6] Incidence is high among young adults, presumably attributed to an adventurous life-style and ingestion of higher volumes of contaminated food.[7]

Chemoprophylaxis. Bismuth subsalicylate preparations (two tablets chewed four times a day) are effective in prevention and treatment of travelers' diarrhea. Taking bismuth subsalicylate will cause passage of black stools, which can be confused with malena. The usual prophylaxis dose of bismuth subsalicylate is approximate to taking 3 to 4 adult aspirins, and hence, this regimen must be avoided by patients on oral anticoagulants. Patients should be advised to rinse their mouths after chewing tablets to avoid black coating of the tongue.

Antimicrobial prophylaxis is not recommended for every traveler. The protective efficacy of an antimicrobial is variable and depends on both the agent used and the duration of treatment. Protection is limited to the time of administration. In addition, individuals are at risk of acquiring diarrhea after the discontinuation of the antibiotic. Antimicrobial prophylaxis can also give a false sense of security and delay physician evaluation and medical treatment when needed.

Antimicrobial prophylaxis should be considered for immunocompromised patients in whom enteric infections are associated with a significant morbidity. These patients

TABLE 2.—*Some Important Travel Related Information Resources*

International Association for Medical Assistance to Travelers (IAMAT). 417 Center Street, Lewiston, NY 14092. Telephone: (716) 754-4883. http://www.cybermall.co.nz/NZ/IAMAT/	Publications include detailed information on tropical diseases, vaccination, climate charts, and the directory of IAMAT physicians, which guides members to travel centers and English-speaking participating physicians in 125 countries and territories.
Travel Medicine Advisor published by American Health Consultants 3525 Piedmont Road NE Suite 400, Atlanta, GA 30305. http://www.ahcpub.com/jtcd.html	Travel information includes an eight-page, bimonthly update and a CD-ROM library containing extensive travel information, country maps with immunization information and travel precautions, lists of international health providers, and an international drug reference.
http://www.cdc.gov/	Home page of the Centers for Disease Control and Prevention (CDC). Comprehensive information on travel medicine including reports of recent epidemics.
http://www.who.org/	Home page of the World Health Organization.
http://www.open.gov.uk./cdsc/	Communicable diseases surveillance-UK updated information about recent epidemics.
http://www.tripprep.com/clinics/clindex.htm or AOL Key word Travel	Travel Health online. Provides list of travel clinics throughout the United States and around the world.
http://travel.state.gov/	US Department of State. Travel advisories regarding personal safety.

should be advised to seek prompt medical evaluation if symptoms do not improve. Daily prophylactic quinolones (ciprofloxacin 500 mg once a day or norfloxacin 400 mg once a day) are recommended for immunocompromised travelers for trips lasting less than three weeks.

Self-treatment.[8] Most cases of diarrhea can be adequately treated with over-the-counter antidiarrheal medications and fluid replacement. Stringent dietary adjustments are no longer recommended since diarrhea can be controlled faster with available therapy. Fluids and bland foods are suggested only if the diarrhea continues despite treatment. Milk, fruits, and red meat should be added only when diarrhea stops.

Symptomatic therapy with bismuth subsalicylate (1 ounce every half-hour for a total of 8 ounces) is effective at least 50% of the time. Loperamide (4 mg loading dose, then 2 mg after each loose stool, up to 16 mg/day) is a faster-acting, effective alternative.

Antimicrobial agents have been shown to limit the course of diarrhea and provide considerable relief of symptoms. Trimethoprim and sulphamethoxazole combinations are no longer the preferred agents in view of worldwide resistance. Fluroquinolones (ciprofloxacin 500 mg twice a day or norfloxacin 400 mg twice a day for three days) are the most effective antibiotics for treatment of travelers' diarrhea. A 3-day course of a quinolone for self-therapy can be prescribed for traveling patients. Unless patients are traveling in the winter months, when *Campylobacter jejuni* diarrhea (for which 3-day quinolone treatment is recommended) is more common, travelers should take one dose of antibiotic and reevaluate themselves after 12 hours. If unformed stools are still passed, the 3-day course has to be completed.

A logical approach to treatment of travelers' diarrhea would be to use bismuth subsalicylate or loperamide for mild (1–2 stools/day) or moderate diarrhea (≥3 stools/day) with no distressing symptoms. For worsening diarrhea with distressing symptoms, the quinolones can be used.

Malaria

Malaria is prevalent in many parts of the world and is becoming increasingly chloroquine resistant. More than 3 million deaths due to malaria are reported annually.[9] A substantial incidence of the disease has been reported in US travelers who did not receive appropriate prophylaxis. Malaria is characterized by high fever with chills. Travelers should be advised to seek prompt medical attention if these symptoms occur up to a year after foreign travel.

Currently, three medications are available for prophylaxis against malaria (Table 3). Chloroquine is recommended for travel to Mexico, Central America, and a few parts of the Middle East where the malarial parasite is still chloroquine sensitive. Mefloquine is the drug of choice for travel to areas with chloroquine-resistant malaria. Nausea and dizziness, often reported side-effects of mefloquine, can be avoided by taking the drug before sleep. Some patients cannot take mefloquine. Patients who have a seizure disorder or are taking drugs which delay cardiac conduction, like quinidine and beta-blockers, should avoid mefloquine. Doxycycline is a reasonable alternative to mefloquine for such patients. A recent study on Indonesian soldiers demonstrated comparative efficacy of mefloquine and doxycycline.[10] Although mefloquine is taken just once a week, doxycycline has to be taken every day. Doxycycline should not be used by pregnant women during their entire pregnancy, children under 8 years of age, and travelers with a known hypersensitivity to doxycycline. Doxycycline can cause significant photosensitivity.

Insect Repellants. The appropriate use of insect repellants is one way of reducing the incidence of malaria. DEET (N, N-diethyl-3-methylbenzamide) is an effective repellant. Repellants containing 25%–30% DEET provide adequate protection.[11] The American Academy of Pediatrics recommends that repellants used on children should not contain more than 10% DEET[10] to avoid neurotoxicity. The repellant must be applied lightly on the skin, and the directions for use in the label of the repellant container should be followed. Permethrin, a synthetic pyrethroid, is an effective insecticide that can be applied to clothing but *not* to the skin.[12] A combination of DEET, which is applied to the skin, and permethrin, which is applied to clothing or window screens, significantly reduces mosquito bites.

Commonly Used Vaccines

An immunization history is an essential part of a traveler's evaluation (Table 4). Hepatitis A, typhoid fever,

TABLE 3.—*Chemoprophylaxis for Malaria*

Drug	*Dosing regimen*	*Precautions*
Chloroquine	500 mg PO once a week. Start one week before travel and continue for four weeks after return.	Ocular side effects. G6PD deficiency.
Mefloquine	250 mg PO once a week. Start one week before travel and continue for four weeks after return.	Avoid in patients with seizures, psychiatric disorders, patients on cardiac drugs like quinidine, propranolol.
Doxycycline	100 mg PO QD. Start one day before travel and continue for four weeks after return.	Avoid in pregnancy, children under eight years of age. Photosensitivity.

PO = by mouth, QD = every day

TABLE 4.—*Vaccinations for Travel*

Vaccine/Immune-globluin	*Dosing Schedule*	*Comments**	*Booster Intervol*
Hepatitis A vaccines	Havrix®Adults: 1440 El U IM Vaqta®: Adults 50 units IM	Inactivated Havrix ® contains 2 phenoxyethanol as preservative. For both vaccines, the most common side effects are mild problems that usually disappear within one to two days.	Adults: 6 to 12 months later
Immunoglobulin for hepatitis A	<3 months: 0.02 ml/Kg-IM >3 months: 0.06 ml/Kg-IM	Avoid concurrent live vaccines.	Repeat every five months
Hepatitis B (Engerix B®)	Accelerated: three doses at 0, 30 and 60 days Standard: three doses at 0, 1 and 6 months	Teenagers may not need vaccination as hepatitis B vaccination has been included in the childhood immunization program.	Accelerated: 12 months Standard: Not known
Yellow fever	0.5 ml SC at least 10 days before travel	Live attenuated virus. Avoid in pregnant patients, patients with severe egg allergy, and immuno-suppressed patients.	Repeat every 10 years
Typhoid fever	Oral: One capsule every other day, four doses. Injectable: ViCPS vaccine, one dose IM Inactivated (heat-phenol) injectable: two doses, four weeks apart	Oral: live attenuated strain *ty21a* strain. Avoid in acute febrile or GI illness. ViCPS: ViCPS vaccine contains phenol- caution in patients with thrombocytopenia, coagulopathies, pregnancy (Category C), immunocompromised states. Inactivated: Reactions following vaccination like fever, myalgias and soreness at injection site are more common than the single dose ViCPS vaccine.	Oral: five years ViCPS: two years Heat-phenol inactivated: three years
Polio	Unvaccinated: three doses IM or SC, one month apart. Completed vaccination: one booster dose	Enhanced-potency inactivated poliovirus vaccine preferred in adults pregnancy (Category C), Avoid in patients with hypersensitivity to neomycin, streptomycin or polymixin B.	
Cholera[18]	Two doses IM or SC, one or more weeks apart	Limited efficacy—50%. Give at least three weeks after yellow fever vaccine.	Six months
Meningococcus	One dose SC	Needed for travel to Saudi Arabia.	None but three years later in high risk groups

IM = intramuscular, SC = subcutaneous

*Allergic reactions can occur due to the vaccine component. History of allergic reactions to vaccines should be evaluated prior to vaccination.

and yellow fever are some of the diseases that can cause significant morbidity and mortality during travel to disease-prevalent areas. Current, childhood and adolescent routine immunization recommendations do not include vaccinations against such diseases.[13] In addition to vaccination, information about food and water precautions should be discussed with the traveler.

Hepatitis A

Hepatitis A is highly endemic throughout the developing world but rarely seen in developed countries such as the United States, Canada, countries in northern and western Europe, Japan, Australia, and New Zealand. Hepatitis A vaccines and immunoglobulins afford excellent protection and are well tolerated.

There are two hepatitis A vaccines currently available in the United States, HAVRIX® and VAQTA®. Both are inactivated vaccines. HAVRIX® contains 2-phenoxyethanol as a preservative. The common side effects of both vaccines are mild and usually disappear within one to two days.

Vaccine Dosage[14]:

HAVRIX®: Adults: Two doses—1440 Elisa Unit (EL.U.) with the second dose administered 6 to 12 months after the first dose.

VAQTA®: Adults: Two doses—50 unit (U) with the second dose administered 6 months later.

Children over the age of two years can receive the vaccination, and multiple regimens are available for children and adolescents. Travelers are considered to be protected four weeks after receiving the initial vaccine dose. The vaccine is estimated to afford protection for about 20 years with the booster dose.

Short-term visitors, children less than two years old, and travelers seen within two weeks of the departure date should receive immunoglobulin.

Yellow Fever

Yellow fever is a viral disease transmitted to humans by mosquito bites. Symptoms range from fever, chills, headache, and vomiting to jaundice, internal bleeding, and kidney failure. Yellow fever has been reported in

unvaccinated visitors to endemic areas. Hence, vaccination is strongly recommended.[15] Many African and South American countries require yellow fever vaccination for entry. In general, even when not required, travelers to tropical Africa and South America should consider yellow fever vaccination.

The vaccination is contraindicated in infants less than four months of age, immunocompromised patients, persons severely allergic to eggs, and pregnant women, who should be advised not to travel to an endemic area. In addition to the vaccine, travelers should use measures to reduce exposure to mosquitoes and protect themselves from mosquito bites. No serious vaccine-related, adverse experiences were observed during clinical trials.

Typhoid Fever

Typhoid fever is a common bacterial infection of the developing world. Typhoid fever is transmitted through contaminated food and/or water, or directly between people. Symptoms of typhoid include high fever, sometimes with chills, coated tongue, headaches, tiredness, loss of appetite, and constipation. Following the food and water precautions closely can reduce the incidence of typhoid fever significantly. One oral vaccine and two injectable vaccines are available. These vaccines provide protection with a 70%–90% efficacy rate.

The oral vaccine consists of four capsules taken every other day over a seven-day period. Protection starts five days after the last dose, and protection lasts about five years. Reactions are rare and include nausea, vomiting, abdominal cramps, and skin rash. In order to maximize the efficacy of oral typhoid vaccine, concomitant use of antibiotics should be avoided; all the four doses should be taken on empty stomach; and the capsules should be refrigerated.[16] A new, one-dose, injectable ViCPS vaccine is now available, which is better tolerated than the old, killed vaccine.

Cholera

Cholera is an acute diarrheal illness caused by infection of the intestine with the bacterium *Vibrio cholerae*. The infection is often mild or without symptoms, but sometimes it can be severe. Approximately 1 in 20 infected persons has severe disease characterized by profuse watery diarrhea and vomiting, often with leg cramps.

The risk of cholera to US travelers who follow food and water precautions is low, and the vaccine is only about 50% effective. As a result, the vaccine is used infrequently even when traveling to areas where epidemics have been reported. Cholera vaccine is not recommended for infants under six months old or for pregnant women.

Meningococcal Meningitis

Meningitis is a bacterial disease characterized by headaches, stiff neck, fever, and a typical rash. Sporadic meningococcal outbreaks have been reported in many underdeveloped countries due to overcrowding. Visitors to areas of high meningitis occurrence are strongly recommended to receive the vaccination. Haj pilgrims to Saudi Arabia are required to be vaccinated against meningococcal meningitis. A tetravaccine is available and affords reasonable protection.

Other Vaccinations

A complete immunization history should be elicited. Travelers should have been immunized against hepatitis B, poliovirus, MMR, diphtheria, and tetanus. Unvaccinated and partially vaccinated persons should receive appropriate vaccinations before traveling. About 10% of the polio cases between 1975 and 1984 were among US citizens returning from foreign travel.[17] Enhanced potency inactivated poliovirus vaccine is preferred for adults. Unvaccinated adults should receive three doses of the polio vaccine, four weeks apart. If travel is unavoidable within the three-month period, two doses, four weeks apart or at least one dose should be given and the series completed on return. Vaccinated adults over the age of 50 or patients who are on immunosuppressive medications should be considered for polio booster vaccinations.

In addition, certain travelers may need protection against Japanese B encephalitis and rabies. Since rabies vaccination does not afford complete protection but only decreases the number of post-exposure vaccination doses, travelers should be cautioned against contact with dogs in areas with high rabies incidence. For diseases such as dengue fever, no vaccines are available, and limiting mosquito bites either with repellants or other measures is the only option available.

Tick-borne encephalitis is prevalent in Europe and the former Soviet Union. Risk of transmission to routine travelers is low. Travelers planning to camp in the woods or explore remote areas should, in addition to vaccination, use protective clothing that covers the arms and legs, use repellants, and inspect the body daily for ticks, complying with instructions for removing attached ticks.[19]

Infections such as anthrax can be acquired abroad due to ingestion of contaminated meat, inhalation of aerosols containing anthrax spores, or cutaneous exposure to contaminated wool or fur. A killed vaccine is available for people with occupational hazards, but is not routinely recommended for travelers. The vaccine series consists of three doses given two weeks apart, with booster doses at 6 months and then on an annual basis.

Epidemics of plague have occurred sporadically. Vaccination, which consists of three injections over six months, is recommended for biologists and workers in plague endemic areas.

Diabetic Traveler

Vaccine recommendations are not different for the diabetic traveler. During long flights, hypoglycemia may occur due to inappropriate dosages. Glucometers and insulin pumps are known to malfunction at high altitudes. The traveling diabetic should carry twice the amount of medications and supplies and pack half of them in the carry-on bag. A snack box containing fruit juices, crackers,

and glucose tablets is an essential part of the diabetic's hand luggage. Using charts and schedules to adjust insulin doses during travel has not been found to be effective. An individualized insulin regimen coupled with simplified advice to inform the airlines about diabetes, monitor blood glucose frequently, and carry carbohydrates to avoid hypoglycemia can be helpful during air travel.

Travelers with HIV

The care of an immunocompromised traveler is complex and has to be addressed carefully.[20] Benefits of the travel should be weighed against the potential health risks. Primary care physicians taking care of HIV patients should advise continued compliance to antiretroviral therapy; warn against the likelihood of developing other diseases, both opportunistic and sexually transmitted; and refer the patients to a travel medicine consultant as soon as travel plans are discussed or at least eight weeks prior to travel. Health and evacuation insurance and access to reliable health services abroad should be discussed.

Some countries may require HIV testing results. In addition to obtaining information from the respective embassies, travelers can log on to the Centers for Disease Control (CDC) travel information site on the World Wide Web at http://www.cdc.gov/travel or the US Department of State site at http://travel.state.gov to obtain entry requirements confidentially.

Vaccinations for the HIV Patient. Routine vaccinations include Pneumococcal vaccine, Hepatitis B series and the yearly influenza vaccine. Generally, live vaccines must be avoided in patients with CD4 counts of less than 200 cells/mm^3. Hepatitis A vaccines, killed cholera vaccine, inactivated typhoid vaccines, and polyvalent meningococcal vaccine can be administered safely. Live viral vaccines, such as oral polio vaccine, MMR, yellow fever vaccine, and live cholera vaccine should not be administered to HIV patients with CD4 counts of less than 200 cells/mm^3. The efficacy of vaccines against rabies, plague, Japanese encephalitis, and tick-borne encephalitis in the compromised traveler are not clear.

Chemoprophylaxis for malaria should be used as it is for immunocompetent travelers. However, drug interactions with protease inhibitors and other new anti-retrovirals are continually increasing in number, and drug interactions should always be considered before prescribing any medication.

Enteric Infection in the HIV-Infected Traveler. Salmonella typhimurium, which causes diarrhea with acute bacteremic febrile illness, is more common in HIV-infected patients and has a high mortality in developing countries. Common protozoal infections due to *Giardia* and *Entamoeba* species are not significantly affected by HIV infection. However, coinfection with helminthic infection can cause severe disseminated disease. Strongyloidiasis, schistosomiasis, and cysticercosis have all affected the HIV traveler and must be considered by the primary care physician when caring for a returned HIV patient with worsening or new symptoms.

Food and water precautions should be strictly adhered to. Bottled water that meets European Union standards, and water that has been treated by distillation, ozonization, or reverse osmosis can be considered safe. Patients with CD4 counts of less than 500 cells/mm^3 on trips of less than three weeks can be placed on daily quinolone prophylaxis. HIV patients developing bloody diarrhea or fever with diarrhea, however, should be advised to seek prompt medical attention.

Patients should be advised to avoid activities that can increase their chances of infection by additional subtypes of HIV, which can accelerate HIV disease progression. Leishmaniasis and trypanosomiasis are emerging as opportunistic infections in addition to the list of already well-known opportunistic infections. Use of insect repellants can reduce the incidence, but patients must be advised to get medical advice if new symptoms occur.

Conclusion

Each year, millions of people travel for business and pleasure. Although traveling is an exciting and informative experience, it also brings certain challenges and risks. International travel, especially to developing countries, can expose people to infectious diseases that are not commonly seen in the United States.

The medical concerns of travelers can be as varied as their itineraries: The need for preventative medications and immunization; the proper way to handle acute and chronic medical illness; the information and documentation that should be taken while traveling; and ways to seek medical assistance abroad are among the varied concerns.

The international traveler should seek medical advice at least four to six weeks prior to his or her departure date. Planning may start even earlier for trips that cover many different countries or that last for extended periods. Travelers with complex medical problems also have reason to plan earlier, and such patients may be referred to a travel medicine specialist. Taking time to plan ahead can help minimize the risks associated with international travel.

REFERENCES

1. Wilson ME. Population movements and emerging diseases. J Travel Med 1997; 4:183–186

2. Ryan CA, Hargrett-Bean NT, Blake PA. *Salmonella typhi* infections in the United States, 1975–1984: increasing role of foreign travel. Rev Infect Dis 1989; 11:1–8

3. Steffen R, Kane MA, Shapiro CN, Billo N, Schoelhorn KJ. Epidemiology and prevention of hepatitis A in travelers. JAMA 1994; 272:885–889

4. Dardick KR. General advice and medical kit. Med Clin North Am 1992; 76:1261–1274

5. Freedman DO. Keeping current: travel medicine resources available on the internet. Infect Dis Clin North Am 1998; 12:543–554

6. Cook JC. Tropical gastroenterological problems. In Cook JC (Ed). Manson's Tropical Diseases (20th ed). London, Saunders, 1996, pp 29–76

7. Okhusyen PC, Ericson CD. Travelers' diarrhea. Med Clin North Am 1992; 76:1357–1373

8. Ericsson CD. Travelers diarrhea: epidemiology, prevention and self-treatment. Infect Dis Clin North Am 1998; 12:285–303

9. Ohrt C, Richie TL, Widjaja H, et al. Mefloquine compared with doxycycline for the prophylaxis of malaria in indonesian soldiers: a randomized, double-blind, placebo-controlled trial. Ann of Intern Med 1997; 126:963–972

10. Fradin MS. Mosquitoes and mosquito repellants: a clinician's guide. Ann Intern Med 1998; 128:931–940

11. Steffen R, Lobel HO. Travel medicine. In Cook JC (Ed). Manson's Tropical Diseases (20th ed). London, Saunders, 1996, pp 407–420

12. Kemp ED. Bites and stings of the arthropod kind. Postgrad Med 1998;103:88–104

13. Immunization of adolescents. MMWR Morb Mortal Wkly Rep Suppl 1996; 45(RR-13):1–13

14. Prevention of hepatitis A through active or passive immunization: recommendations of the advisory committee on immunization practices (ACIP). MMWR Suppl. 1996; 45(RR-15):1–30

15. Cryz SJ Jr. Yellow fever vaccine. MMWR Morb Mortal Wkly Rep 1990; 39:1–6

16. Cryz SJ Jr. Patient compliance in the use of Vivotif Berna® vaccine, typhoid vaccine, live oral Ty21 a. J Travel Med 1998;5:14–17

17. Poliomyelitis–United States, 1975–1984. MMWR Morb Mortal Wkly Rep 1986; 35:180–182

18. Jong EC. Immunizations for international travelers. Med Clin North Am 1992; 76:1277–1294

19. Jong EC. Immunizations for international travel. Infect Dis Clin North Am 1998; 12:249–266

20. Mileno MD, Bia FJ. The compromised traveler. Infect Dis Clin North Am 1998; 12:369–412

Articles

Amebic Liver Abscess: Epidemiology, Clinical Features, and Outcome

REGINALD K. SEETO, MB, BS, *San Francisco, California; and* DON C. ROCKEY, MD, *Durham, North Carolina*

Amebic liver abscess (ALA) is a serious, but readily treatable form of hepatic infection. In order to understand the clinical features of this condition in the United States, we reviewed the medical histories of 56 patients with ALA at two large San Francisco Hospitals from 1979 to 1994. Patients were divided into the following groups based on the presumed manner in which they had acquired ALA: those born or raised in the United States, with a history of travel to an endemic area (Tr-ALA); those from an endemic area, but living in the United States for less than one year (En-ALA); and those neither from nor having traveled to an endemic area (N-ALA). We found distinct clinical patterns in patients from different epidemiological groups. Patients with Tr-ALA were a decade older than those from endemic regions, were more likely to be male, and tended to have an insidious onset. Furthermore, compared to patients with En-ALA, those with Tr-ALA were more likely to have hepatomegaly ($P < 0.0001$) and large abscesses (ALA >10 cm; $P < 0.01$). One third of the patients studied had no associated travel history or endemic origin as risk factors. Of these, 63% had a condition consistent with severe immunosuppression, such as infection with the human immunodeficiency virus (HIV), malnourishment with severe hypoalbuminemia, or chronic infection. In patients with N-ALA, the presence of a presumed immunosuppressed state increased significantly, as compared to patients with endemic or travel risk factors for ALA. During the last five years of the study, one third of all patients diagnosed with ALA were HIV positive (including 2 with a new diagnosis of AIDS), many of whom were discovered to be HIV-infected only after presentation with ALA. We conclude that travel to and origin in an endemic area are important risk factors for the development of ALA, and patients in these different epidemiological groups appear to have distinct clinical features. Further, in the absence of recognized risk factors, the development of ALA may suggest an immunocompromised host.

(Seeto RK, Rockey DC. Amebic liver abscess: epidemiology, clinical features, and outcome. West J Med 1999; 170:104–109)

Infection with the parasite *Entamoeba histolytica* is common worldwide. Most patients infected with *Entamoeba histolytica* have only colonic symptoms and signs. Although less common than colonic amebiasis, extra-intestinal amebiasis is often more consequential. The most frequent form of extra-intestinal amebiasis is amebic liver abscess (ALA), which may develop serious complications if not rapidly detected and properly managed. With appropriate management, however, patients with ALA have an excellent prognosis.[1]

Although *Entamoeba histolytica* infection is most common in underdeveloped countries, immigration and the modernization of transport have contributed to an increased incidence and awareness of ALA in developed countries, such as the United States. Therefore, the aim of this study was to investigate the clinical features of patients with ALA in the United States. We report on a large cohort of patients with ALA and address both the epidemiologic profiles and clinical characteristics of patients with ALA in this setting.

Methods

Amebic liver abscess was identified in 56 patients between January 1, 1979, and December 31, 1994, at two hospitals affiliated with the University of California, San Francisco, Moffit-Long Hospital and San Francisco General. Each ALA was confirmed by radiological or surgical demonstration of an intrahepatic abscess cavity and by positive amebic serology. A presumptive diagnosis of ALA was made in two patients; amebic serology was not performed, but each had amebic stool cysts and a rapid clinical response to antiamebic treatment. In one patient, a histopathologic diagnosis of disseminated amebiasis

From the Departments of Medicine/Divisions of Gastroenterology, University of California, San Francisco, California (Dr Seeto), and Duke University Medical Center, Durham, North Carolina (Dr Rockey).

Reprint requests to Don C. Rockey, Liver Center, Sands Building, Room 334, Duke University Medical Center 3083, Durham, NC 27710 (e-mail: dcrockey@acpub.duke.edu).

TABLE 1.— *Epidemiological Features in 56 Patients with ALA* *

Features†	*Endemic (En-ALA)*	*Travel (Tr-ALA)*	*No risk factors (N-ALA)*
Number	27	13	16
Age, y†	28 (19–70)	40 (23–67)	36 (1–52)
Female:Male	5:22	0:13	2:14
Born in USA (%)	0 (0%)	3 (23)	13 (81)
Symptoms PTA, d‡	9 (1–120)	28 (2-180)	14 (3–60)
Symptoms > 1 mo (%)	8 (30%)	7 (54%)	2 (13%)
Hospitalization, d	7 (3–19)	8 (3–18)	8 (3–38)
Defervescence, d	2 (1–9)	3 (1–7)	3 (1–9)
Ethanol (%)§	11 (41)	9 (69)	4 (25)
HIV positive (%)	0 (0)	0 (0)	6 (38)#
Malnutrition (%)‖	2 (7)	3 (23)	2 (13)
Tuberculosis (%)	3 (11)	2 (15)	3 (19)
Immunosuppressed (%)¶	5 (19)	4 (31)	10 (63)**
Immunosuppressed and/or ethanol (%)	15 (56)	9 (69)	12 (75)

PTA = prior to admission

*Patients with En-ALA were born and had lived the majority of their lives in an endemic region and had been in the United States for less than one year. Patients with Tr-ALA were born in the USA or had lived the great majority of their lives in the USA and had traveled on one occasion to an endemic region. Patients with N-ALA were neither from nor had traveled to an endemic area.

†Numbers of patients in each group are shown, numbers in parentheses represent the percent of the total number in each specific subgroup (i.e. En-ALA, Tr-ALA and N-ALA), except where a range is shown.

‡Symptoms were any of those listed in Table 2.

§Heavy ethanol consumption was defined as > 150 grams ethanol/day.

‖Has evidence of wasting with severe hypoalbuminemia (<2.6 grams/dl) not due to any other cause (i.e. cardiac, liver, or renal failure).

¶An immunosuppressed condition was considered to be present in patients with HIV infection, infection with *Mycobacterium tuberculosis*, or with malnutrition and hypoalbuminemia (albumin <2.6 g/dL) not due to other causes.

#$P < 0.01$ compared to either En-ALA or Tr-ALA.

**$P < 0.001$ versus En-ALA group.

was made at autopsy. Specimens for parasitology were collected from fresh stools or drainage from interventional radiology or surgery. Patients with non-amebic etiologies for liver abscesses were excluded. Substantial alcohol consumption was considered to be present when ingested ethanol was >150 grams/d. A state of clinical immunosuppression was defined by the presence of either of the two following conditions: severe clinical malnutrition with muscle wasting and an albumin level of less than 2.6 gram/dl, demonstrated by physical and laboratory examination and having no other potential cause; or a serious, chronic, underlying infection, such as tuberculosis or HIV infection. Recurrence was defined as an ALA appearing subsequent to initial clinical or radiographic resolution.

We defined the following epidemiologic profiles: Endemic ALA (En-ALA) occurred in patients born and living the majority of their lives in an endemic region, who had been in the United States for less than one year. In this study, 16 patients came from Mexico, 7 from Asia, and 4 from South America. ALA occurring after travel (Tr-ALA) occurred in patients born or having lived the majority of their lives in the United States, who had a reported history of travel to a country where amebiasis is endemic. In this study, eight had travelled to Mexico, four to Asia, and one to South America. The final epidemiologic group was considered to be those neither from nor having traveled to an endemic area (N-ALA). Acute and chronic ALA were defined by the presence of symptoms for less than or more than 14 days, respectively. Statistical analyses were performed with either Fisher's exact test or the Student's *t* test. This study was approved by the Committee on Human Research of the University of California, San Francisco and was performed in accordance with the guidelines set forth in the Declaration of Helsinki[2] for ethical conduct in the study of human subjects.

Results

Epidemiology and Etiology

In this series, the incidence of ALA was 8.5 patients/100,000 hospital admissions. Of those diagnosed, 75% were young men born outside the United States, and only 18% of patients were older than 50. We segregated ALAs by etiology (Table 1). The median time to presentation after travel was 20 weeks, with a range of 2 to 60 weeks. One third of all patients with ALA had associated medical conditions. Eight had tuberculosis, three had syphilis, three had hepatitis C, three had peptic ulcer disease, one had diabetes mellitus, and one had had a posttraumatic splenectomy. In addition, 43% of the patients studied had a history of heavy alcohol consumption.

Patients with travel-related ALA were all men, many with histories of significant alcohol consumption. Tr-ALA patients were older than patients with En-ALA, and Tr-ALA presented subacutely in comparison with all other ALAs (Table 1). ALA was more prevalent in

TABLE 2.—*Symptoms and Signs at Presentation in 56 Patients with ALA*

Finding	*Number*	*%*
Symptoms		
Abdominal pain*	47	84
Fever	45	80
Chills	41	73
Nausea, vomiting and/or anorexia†	36	64
Sweats	32	57
Pleurisy, shortness of breath, and/or cough††	23	41
Diarrhea§	16	29
Weight loss‖	16	29
Signs		
Fever¶	47	84
Abdominal tenderness	45	80
Hepatomegaly (>14 cm)	14	25
Respiratory findings#	14	25
Guarding or rebound	11	20
Jaundice	2	4

*Pain was located in the following areas: right sided (31), epigastric (7), diffuse (4) or not stated (5). Pain was referred to the following areas: back or flank (9), shoulder (7) and chest wall (2).

†There were 23, 22, and 18 patients with nausea, anorexia and vomiting, respectively.

††There were 13, 8 and 8 patients with pleurisy, shortness of breath and cough, respectively.

§Bloody diarrhea was recorded in 5 patients.

‖Median weight loss was 20 lb (range 5-40 1b). There was a statistically significant difference for weight loss between ALA with an acute and chronic presentation (11% versus 60%, respectively) with $P < 0.0004$ (Fisher's exact test).

¶There were 31 high grade (>38.5°C) and 16 low grade (37.5<T<38.4°C) temperatures. Three initial temperature readings were not available. All patients afebrile on admission became febrile during admission.

#Respiratory findings included decreased breath sounds, dullness to percussion or added sounds.

men than women in all groups. In the N-ALA group, there were six homosexual male patients, three of whom also used intravenous drugs. Three of these patients were known to be HIV-infected prior to admission, and three were diagnosed after their clinical presentation with ALA. Of note, the five HIV-infected patients who presented between 1990 and 1994 accounted for one third of all ALA cases during that time period. Other conditions associated with immunosuppression included tuberculosis, severe malnutrition with severe hypoalbuminemia (<2.6 g/dl) in the absence of other causes, splenectomy and diabetes (Table 1). The presence of HIV was significantly greater in patients with N-ALA than in other ALA groups (versus En-ALA $P < 0.001$; versus Tr-ALA $P < 0.02$). Similarly, the presence of an immunosuppressed state in patients with N-ALA was also significant (versus En-ALA and Tr-ALA patients, $P < 0.01$).

Clinical Features

Symptoms were generally nonspecific (Table 2), but a large proportion of patients presented with fever and pain in the right upper quadrant; both symptoms were present in 72% of patients. Physical signs reflected symptoms (Table 2). All afebrile patients exhibited an elevation in temperature during admission. Notably, 83% of all fevers were high grade. Defervescence occurred rapidly in most patients (median 2.5 days, range 1–9 days), except HIV-infected patients, whose fevers lasted three times longer than other patients'. Of all patients with ALA, 39% had anorexia, and 29% had weight loss. Only five patients reported bloody diarrhea. Jaundice was extremely rare.

The median duration of symptoms prior to presentation was relatively short, although 30% of patients had symptoms for at least 30 days. The majority of patients with En-ALA (63%) and N-ALA (82%) had a short duration of symptoms prior to admission (<14 days), and 90% were discharged within 2 weeks of admission. By contrast, Tr-ALA patients had an indolent course with more than 50% having symptoms lasting over 1 month prior to presentation (Table 1). The presentation of patients with En-ALA was notable for the presence of fever and abdominal tenderness (93%). Nausea (48%), vomiting (44%), and pleurisy (30%) were most frequently observed in patients with En-ALA. Of N-ALA patients, 88% had a significant history of fever and chills, and 93% had high-grade temperatures during admission. Only two thirds, however, reported a history of abdominal pain. On admission, Tr-ALA patients were least likely to be febrile or exhibit abdominal tenderness, but were most likely to display constitutional symptoms (80% sweats, 31% myalgias, 23% headaches), hepatomegaly (69%) and respiratory findings (40%). Hepatomegaly was found four and ten times more often in patients with a travel history than in patients with N-ALA or En-ALA, respectively. Moreover, constitutional symptoms (sweats, myalgias, headaches, $P < .05$) and hepatomegaly were more common in Tr-ALA than En-ALA (69% versus 7%, $P < 0.0001$), although abdominal tenderness was less frequent (62% versus 93%, $P < .02$).

Laboratory Findings

The white blood cell count (WBC) was elevated in 70% of patients ($15 \pm 1 \times 10^9$/liter), and 10% had WBC $> 20 \times 10^9$/liter). Serum liver tests were generally unremarkable and were as follows (mean + SEM): albumin 3.4 + 0.2 grams/dl (normal >3.3); total bilirubin 1.0 + 0.1 mg/dl (normal <1.2); alanine transaminase (ALT) 52+7 U/liter (normal <40); aspartate transaminase (AST) 44 + 8 U/liter (normal <50); alkaline phosphatase (SAP) 159 + 12 U/liter (normal <115). No patient had a bilirubin level >3.2 mg/dl, though 20% of patients had levels >1.2 mg/dl. Two fifths of patients had hypoalbuminemia with none having levels <1.9 grams/dl. One third had an underlying anemia (12.8 ± 0.3 grams/dl), but severe anemia was uncommon.

Imaging

Chest and abdominal plain films were nonspecific (Table 3). The sensitivities of computed tomography (CT) and ultrasonography (US) in detecting ALA were 100% and 85%, respectively (Table 3). The five ALAs missed by US were confirmed by two repeat USs, one CT, one

TABLE 3.—*Initial Radiographic Imaging in 56 Patients with ALA**

Features	*Number*	*%*
Abnormal chest x-ray†	21	44
Abnormal abdominal x-ray††	17	52
Abnormal abdominal US§	47	90
<5.0 cm	14	25
5–10 cm	25	45
>10 cm	13	23
Abnormal abdominal CT scan	23	100

US = ultrasound and CT = computed tomography

*Available images included 48 chest X-rays, 33 plain abdominal films, 52 ultrasounds, 23 CT scans.

†There were 13 patients with a pleural effusion, 13 with elevated right hemidiaphragm, and 12 with atelectasis. Some studies had more than one abnormal finding.

††There were 9 patients with a sentinel loop, 6 with air fluid levels, five with hepatomegaly, and 1 with free air under the diaphragm. Some studies had more than one abnormal finding.

§If multiple ALAs were present, then the largest was measured.

TABLE 4.—*Location and Number of Amebic Abscesses*

Feature	*Number*	*%*
Location of ALA		
Right lobe	44	79
Left lobe	5	9
Both lobes (left, right, caudate)	5	9
Caudate	2	4
Number of ALA		
Single	43	77
Multiple	13	23

ALAs were identified by ultrasound, computed tomography or autopsy.

surgery, and one autopsy. Amebic liver abcessess were most often single, located on the right posterior or anterior segment, and <10 cm in size (Table 4). Amebic liver abscessess on the left side were distributed equally between the lateral and medial segments. Of patients with Tr-ALA, 55% had ALAs >10 cm in size. This group accounted for the greatest proportion of multiple ALAs (40%) and ALAs involving the left or both lobes (40%). Patients with Tr-ALA or a chronic presentation were more likely to have an ALA >10 cm (Tr-ALA, 55% versus En-ALA, 22%, $P < .01$; chronic presentation, 47% versus acute presentation, 12%, $P < 0.01$) (Table 4). All six ALAs in HIV-infected patients were right-sided; five were located in the posterior segment.

Microbiology

Amebic serology was performed using the following tests: indirect hemagglutination (IHA) in 37 patients, enzyme-linked immunoabsorbent assay (ELISA) in 15 patients, counterimmunoelectrophoresis (CIE) in 14 patients, latex fixation (LF) in 8 patients, immunodiffusion (ID) in two patients, and complement-fixation (CF) in 1 patient. Of the 77 tests, 5 were initially negative, including 2 IHAs, 2 CIEs, and 1 LF. In 13 out of 43 patients (30%), cultures of stool specimens revealed cysts or trophozoites, either singly or in combination (50%, 37% and 23% in Tr-ALA, En-ALA and N-ALA patients, respectively). Trophozoites were identified in 4% of abscess aspirates. Abscess cultures from two patients grew one contaminant and an *Escherichia coli*. Blood cultures from three patients grew two contaminants and an *Escherichia coli*.

Treatment

All patients received antibiotic treatment: 75% received a combination of metronidazole and diiodoquinol, and 25% received metronidazole alone. Almost half the patients underwent invasive diagnostic or therapeutic procedures, of which percutaneous needle aspiration was the most commonly performed. Of 20 patients who underwent aspiration, 1 developed acute respiratory distress (ARDS). Patients in the N-ALA group were most likely to undergo an invasive procedure (>60%). Defervescence took longer in patients who underwent invasive procedures than in those treated with antibiotics alone (Table 5).

Morbidity and Mortality

Complications included contiguous extension or rupture in 6 (11%) of patients, ARDS after an interventional radiological procedure in 1 (2%), recurrence in 2 (4%) and superinfection in 1 patient (2%). This latter patient, the only patient who died in this series, had *Escherichia coli* septicemia and multisystem organ failure with positive blood and abscess cultures. The diagnosis was not suspected prior to death and only made at autopsy. Patients with Tr-ALA (15%) and N-ALA (13%) were twice as likely as En-ALA (7%) patients to have a contiguous extension or rupture, but the latter had the only recorded death (4%). The recurrence rate was 0% for patients with N-ALA, 4% for patients with En-ALA, and 7% for patients with Tr-ALA. There was no consistent relationship between clinical improvement and a changed radiological appearance.

Discussion

We have identified distinct clinical features in patients with ALA who have different epidemiological profiles. Differences were found in groups of patients developing ALA after travel to an endemic area (Tr-ALA) and those with ALA after living in an endemic area (En-ALA). The former were older and more likely to be male and had a more insidious onset of illness, more marked hepatomegaly, larger ALAs, and a greater proportion of multiple ALAs, including those involving the left or both lobes. These differences in clinical presentation, found in our subgroups, are consistent with differences reported previously between subgroups of patients with either acute or chronic clinical

TABLE 5.—*Specific Treatment in 56 Patients with ALA**

Treatment	*Number (%)*	*Metronidazole (days)†*	*Time to defervesce (days)*
Antibiotics alone	31 (55)	11 (10–28)	2 (1–6)
Simple aspiration	12 (21)	13 (10–18)	4 (1–8)
Percutaneous drainage	8 (14)	15 (10–18)	4 (1–9)
Surgical drainage	5 (9)	17 (10–20)	3 (1–5)

*Median number of days are given with range in parentheses.

†Metronidazole (oral and/or intravenous) was the tissue active antibiotic used in all cases. It was used in combination with an antiluminicidal agent (most commonly a three-week course of Diidohydroxyquin) in 75% of ALA cases. The other 25% were treated with metronidazole alone.

presentations of ALA.[3] Hepatomegaly has also been found to be prevalent in patients who presented subacutely.[3] The longer duration of illness in patients with Tr-ALA may result in greater hepatomegaly and larger abscesses. Despite divergent epidemiological, clinical, and radiological features in patients with ALA in different settings, overall rates of complication, recurrence and mortality were low.

It has been previously proposed that those patients acquiring ALA as endemic residents are more likely to exhibit a chronic than an acute presentation.[3] According to this view, previous exposure and presumed immunization through infection modulate the immunological response, leading to a subacute illness in those with recurrent exposure to *Entamoeba histolytica*. Those with first-time exposure to *Entamoeba histolytica*, on the other hand, are thought to develop an "acute" clinical illness. Our findings do not support this postulate. We found that En-ALA patients had a more acute presentation with symptoms lasting for less than 14 days, while patients with Tr-ALA were most likely to have a chronic presentation, with symptoms lasting for over 1 month). Our patients and those reported earlier did, however, share notably similar clinical features in both "acute" and "chronic" presentations.[3] Indeed, patients with chronic presentation were older and more likely to have weight loss, respiratory findings, hepatomegaly and a positive initial US than patients with an acute presentation, although only differences for weight loss and ALA size were statistically significant. Our data suggest that regardless of epidemiological background, patients with ALA tend to exhibit acute or chronic clinical presentations. Additionally, our findings raise the possibility that "acute" ALA in the En-ALA group may represent a low-level, rapidly evident, and, perhaps, rapidly clearing infection, whereas "chronic" ALA in the Tr-ALA group may represent severe, persistent infection. One alternative postulate to explain the differences in presentations between the different epidemiological groups reported here and previously[3] (that is between the En-ALA and Tr-ALA groups), is that our patients and those reported previously could have been infected with different strains of *Entamoeba histolytica*, which could, in turn, be associated with divergent presentations. This postulate is consistent with a previously proposed hypothesis.[4]

Amebic liver abcess is a relatively uncommon complication of colonic amebiasis. Although the pathogenesis of ALA is not known, it is possible that an altered immune response to *Entamoeba histolytica* could contribute to the development of ALA. Alcohol consumption in particular is an important potential immunosuppressive factor, and it has been reported in up to 80% of patients with En-ALA.[5] Alcohol may make the liver more susceptible to *Entamoeba histolytica* infection by directly impairing Kupffer cell function in the liver or by hindering the cellular and humoral immunologic response to *Entamoeba histolytica*. In this series, over 40% of patients had a history of heavy alcohol consumption, and consumption was highest in patients with Tr-ALA (69%).

Experimental studies have shown impaired immunity to be an important factor in the pathogenesis of ALA.[6–8] Immunosuppression after thymectomy or splenectomy in animals results in an increased incidence of ALA.[6,7] Stimulation of the immune system with bacillus Calmette-GuErin (BCG), however, reduces the risk of developing ALA.[8] Furthermore, iatrogenic exacerbation of ALA in patients unsuspected of harboring ALA has been documented after the administration of corticosteroids.[9,10] In our series, of the 56 patients reported, 16 (29%) had not been placed at risk for ALA by either endemic origin or travel history (N-ALA). Furthermore, 10 of those 16 patients with N-ALA (63%) had an associated condition compatible with severe immunosuppression. These patients had significant medical conditions, such as HIV infection (38%), malnourishment with severe hypoalbuminemia (25%), chronic infections, namely tuberculosis and syphilis (25%), heavy alcohol use (25%), hepatitis (13%), or had undergone splenectomy (6%).

Together, our data and the experimental data raise the possibility that an immunocompromised state could be a risk factor for the development of ALA. It is also possible, however, that invasive amebiasis itself leads to immunosuppression.

Whether HIV infection is a risk factor for development of ALA is unknown. We identified six HIV-infected patients with ALA, two of whom had AIDS by standard criteria. All of the HIV-infected patients were born in the United States, and none had a history of

travel to an endemic area. All six were homosexual. Homosexual men are known to have an increased incidence of colonic amebiasis due to increased fecal-oral contact. During the 1970s, the incidence of amebiasis increased by 8000% in homosexual men in San Francisco[11] over a 10-year period, and 40% of patients with amebiasis in a New York hospital were homosexual.[12] Thus, a homosexual lifestyle appears to facilitate the transmission of *Entamoeba histolytica*. Whether HIV infection in conjunction with the enhanced transmission of *Entamoeba histolytica* increases the risk of ALA remains an open question requiring further study.

The relationship between HIV/AIDS and ALA may be important. In the last five years of our series, one third of all patients with ALA were HIV-infected, and it is notable that three of the six HIV-infected patients were found to be HIV-positive after the ALA was diagnosed (including 2 patients who were found to have AIDS by CD4 criteria). It has been proposed that there could be an increase in extra-intestinal amebiasis, including ALA, in HIV-infected patients due to the emergence of less virulent strains.[13] Although our data suggest that this may be possible, a population-based, epidemiological study comparing an HIV-infected population to a population with travel-related risk and to a population without risk is required. Furthermore, such a study could explore possible differences between strains of *Entamoeba*, such as *Entamoeba histolytica*, the "pathogenic" species, and *Entamoeba dispar*, the "nonpathogenic" species. This study could also investigate the conversion of nonpathogenic strains, presumable prevalent in many homosexual populations,[14] into pathogenic strains, which has been postulated to occur *in vitro*.[15] In any case, the presence of a space-occupying hepatic lesion in an HIV-infected patient should indicate the possible presence of ALA, and the patient should be managed accordingly.

In conclusion, travel to and origin in an endemic area are important risk factors for the development of ALA, and patients in each of these groups appear to have distinct clinical features. In addition, a subset comprising one third of patients in this series had no travel to or origin in an endemic area, but appeared to be susceptible to development of ALA. In this group, the majority had associated immunosuppressive conditions, of which HIV infection was the most common. These data raise the possibility that impaired host immunity may be an important factor in the pathogenesis of ALA. Moreover, from a clinical management perspective, the finding of an ALA in a patient without travel or endemic risk factors should suggest the possibility of a compromised immune system.

Acknowledgments

This study was supported in part by the Thomas and Mary Ethel Travel Fellowship of the University of Sydney, Sydney, Australia (RKS) and by the Confederation of Australian Medical Defense Organizations (CAMDO) Scholarship, Sidney, Australia (RKS).

REFERENCES

1. Nordestgaard AG, Stapleford L, Worthen N, Bongard FS, Klein SR. Contemporary management of amebic liver abscess. Am Surg 1992; 58:315–320

2. World Medical Association Declaration of Helsinki. Recommendations guiding physicians in biomedical research involving human subjects. JAMA 1997; 277:925–926

3. Katzenstein D, Rickerson V, Braude A. New concepts of amebic liver abscess derived from hepatic imaging, serodiagnosis, and hepatic enzymes in 67 consecutive cases from San Diego. Medicine 1982; 61:237–246

4. Reed SL. New concepts regarding the pathogenesis of amebiasis. Clin Infect Dis 1995; 21(Suppl 2):5182–5185

5. Gupta RK. Amebic liver abscess: a report of 100 cases. Int Surg 1984; 69:261–264

6. Ghadirian E, Meerovitch E. Effect of immunosuppression on the size and metastasis of amoebic liver abscesses in hamsters. Parasite Immunol 1981; 3:329–338

7. Ghadirian E, Meerovitch E. Effect of splenectomy on the size of amoebic liver abscesses and metastatic foci in hamsters. Infect Immun 1981; 31:571–573

8. Ghadirian E, Meerovitch E. Macrophage requirement for host defense against experimental hepatic amebiasis in the hamster. Parasite Immunol 1982; 4:219–225

9. Stuiver PC, Goud TJ. Corticosteroids and liver amoebiasis. Br Med J 1978; 2:394–395

10. Kanani SR, Knight R. Relapsing amoebic colitis of 12 year's standing exacerbated by corticosteroids. Br Med J 1969; 2:613-614

11. Pearce RB. Intestinal protozoal infections in AIDS. Lancet 1983; 2:51

12. Schmerin MJ, Gelston A, Jones TC. Amebiasis. An increasing problem among homosexuals in New York City. JAMA 1977; 238:1386–1387

13. Thompson JE Jr, Freischlag J, Thomas DS. Amebic liver abscess in a homosexual man. Sex Transm Dis 1983; 10:153–155

14. Weinke T, Friedrich-Janicke B, Hopp P, Janitschke K. Prevalence and clinical importance of *Entamoeba histolytica* in two high-risk groups: travelers returning from the tropics and male homosexuals. J Infect Dis 1990; 161:1029–1031

15. Mirelman D, Bracha R, Chayen A, Aust-Kettis A, Diamond LS. *Entamoeba histolytica*: effect of growth conditions and bacterial associates on isoenzyme pattems and virulence. Exp Parasitol 1986; 62:142–148

Alerts, Notices, and Case Reports

Yersinia pseudotuberculosis Bacteremia and Splenic Abscess in a Patient With Non–Insulin-Dependent Diabetes Mellitus

W. KIMRYN RATHMELL, MD, PHD
PAUL ARGUIN, MD
Stanford, California
STEPHANIE CHAN, MD
ALBERT YU, MD
San Jose, California

Report of a Case

The patient, a 56-year-old woman with a long history of diet-controlled non–insulin-dependent diabetes mellitus, had a two-week history of fevers, chills, malaise, and loose stools but no abdominal pain. On admission to the hospital, her temperature was 38.5°C. Her abdomen was nontender without hepatosplenomegaly. Her aspartate aminotransferase (AST) level was 103 U per liter; alanine aminotransferase (ALT), 34 U per liter; alkaline phosphatase, 132 U per liter; lactate dehydrogenase (LDH), 1,032 U per liter; leukocyte count, 10.1×10^9 per liter; platelets, 83×10^9 per liter; and an international normalized ratio, 1.6. A urinalysis showed 4 to 10 leukocytes and many bacteria. A week before her hospital admission, her laboratory values were as follows: AST, 30 U per liter; ALT, 25 U per liter; alkaline phosphatase, 89 U per liter; and LDH, 214 U per liter.

She was admitted to the hospital for probable pyelonephritis and treated empirically with a regimen of intravenous gentamicin sulfate and ampicillin. A chest roentgenogram demonstrated elevation of the left hemidiaphragm, which suggested a possible subdiaphragmatic abscess. An abdominal ultrasonogram showed an enlarged, inhomogeneous spleen. An abdominal computed tomographic scan (Figure 1A) demonstrated an enlarged spleen with multiple 1-cm areas of decreased attenuation, suggestive of splenic abscesses. The urine culture grew more than 10^6 colonies of lactobacilli, thought to be a contaminant, and two of four blood cultures grew *Yersinia pseudotuberculosis* on days 4 and 7, which was sensitive to ampicillin, trimethoprim-sulfamethoxazole (Septra), cefazolin, cefotetan, ceftazidime, gentamicin, and tetracycline. Antibody titers were negative for the human immunodeficiency virus, hepatitis B surface antigen, and hepatitis C.

The patient defervesced on hospital day 3 and on hospital day 4 again became febrile. Her platelet count decreased to 35×10^9 per liter on hospital day 3, with a normal panel for disseminated intravascular coagulation, suggesting that she probably had isolated thrombocytopenia associated with her bacteremia. Her platelet count then increased steadily to 164×10^9 per liter by day 10. By hospital day 8, her laboratory values were as follows: AST, 46 U per liter; ALT, 32 U per liter; alkaline phosphatase, 231 U per liter; LDH, 384 U per liter; and leukocyte count, 8.3×10^9 per liter. An abdominal computed tomographic scan after ten days of antibiotic therapy showed persistent multiple 1-cm lesions with some coalescence (Figure 1B). She also continued to be febrile and then had a splenectomy with a partial gastrectomy on day 13 (gastrectomy done to repair gastroduodenal fistula). Cultures of the spleen were negative for pathogens, and the histopathologic examination noted multiple 1-cm nodules containing necrotic tissue and masses of macrophages (Figure 2). After the operation, she received ten more days of ampicillin and gentamicin therapy. At the time of discharge, her laboratory values were as follows: AST, 24 U per liter; ALT, 12 U per liter; alkaline phosphatase, 254 U per liter; and LDH, 303 U per liter.

Discussion

Yersinia species are small gram-negative coccobacilli that grow optimally at cooler temperatures, between 25°C and 32°C. Because these are relatively uncommon pathogens, automated microbiologic identification systems should not be relied on, and speciation is usually determined with manual batteries of biochemical tests. If there is a strong suggestion of infection with a *Yersinia* species, the microbiology laboratory needs to be alerted so that a special culture medium, cefsulodin irgason novobiocin (CIN) plate, can be used. The culture also needs to be grown at room temperature because *Yersinia* species grow better in a cooler environment. Four key reactions differentiate *Y pseudotuberculosis* from *Yersinia pestis*, the causative agent of plague. The former reliably demonstrates motility at room temperature, hydrolyses urea, and ferments both rhamnose and melibiose, whereas *Y pestis* may rarely have a positive reaction to one of these tests.

Yersinia pseudotuberculosis is a rare human pathogen. It is a zoonotic organism carried primarily by rodents, although domesticated farm animals also serve as a reservoir.[1] Most commonly, the infection manifests as a

(Rathmell WK, Arguin P, Chan S, Yu A. *Yersinia pseudotuberculosis* bacteremia and splenic abscess in a patient with non–insulin-dependent diabetes mellitus. West J Med 1999; 170:110–112)

From the Department of Medicine (Dr Rathmell) and the Division of Infectious Diseases (Dr Arguin), Stanford University School of Medicine, Stanford, and the Department of Medicine, Santa Clara Valley Medical Center, San Jose (Drs Chan and Yu), California.

Reprint requests to Albert Yu, MD, Department of Medicine, Santa Clara Valley Medical Center, San Jose, CA 95128.

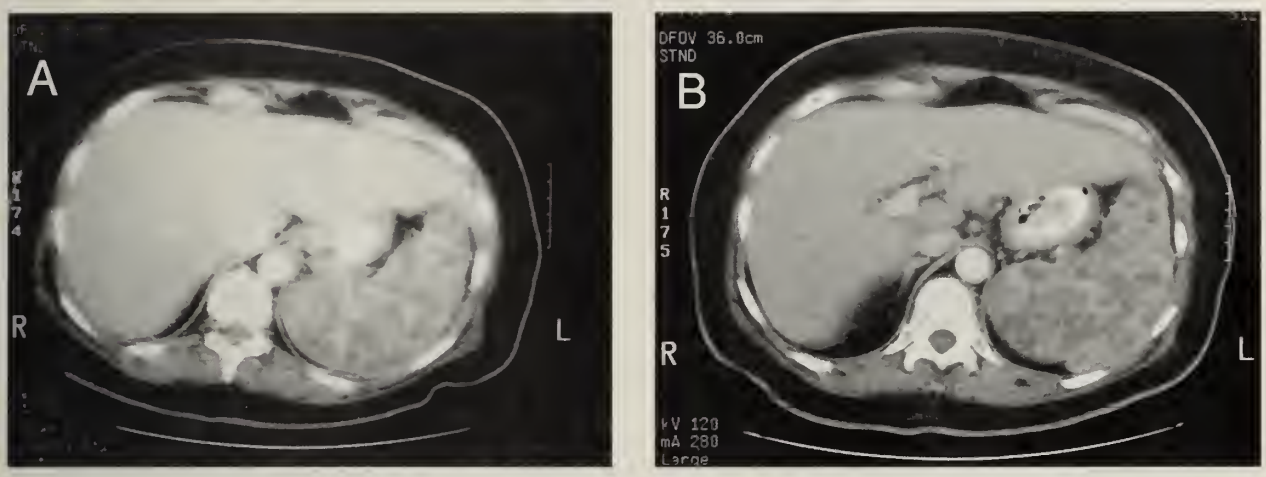


Figure 1.—Abdominal computed tomographic (CT) scans were taken of the spleen. A, A CT scan with contrast medium taken on hospital day 2 reveals multiple sharply demarcated, 1- to 2-cm areas of low attenuation filling the enlarged spleen. B, A CT scan with contrast medium taken after 10 days of treatment demonstrates a slightly smaller spleen with persistent 1- to 2-cm areas of low attenuation, with some coalescence.

mesenteric lymphadenitis with abdominal pain, fever, and diarrhea; in infants and small children, it presents mostly as a nonbloody gastroenteritis.[1] Bacteremia resulting from *Y pseudotuberculosis* infection is rare and usually occurs in patients with underlying disorders such as diabetes mellitus, hepatic cirrhosis, or iron overload.[2] Overall mortality, even with appropriate antimicrobial therapy, has been estimated to be as high as 75%.[1] Only a few patients with diabetes as their sole underlying risk factor have been described.[3,4] Furthermore, although reports of cases involving liver, pulmonary, and suprarenal abscesses have been published, there have been no reports of *Y pseudotuberculosis* as a cause of splenic abscess in a patient with diabetes mellitus.

Splenic abscess itself is another uncommon phenomenon. Autopsy studies suggest that the incidence of splenic abscess is between 0.2% and 0.7%.[5,6] It is, however, a diagnosis increasingly made due to the improved therapies for immunocompromised patients and advancements in diagnostic imaging techniques, particularly computed tomography.[5–9] Underlying illnesses, like diabetes and endocarditis, and various immunodeficiency states are predisposing conditions to the development of splenic abscess.[5,7,8] Causes of splenic abscess include *Staphylococcus aureus*, fungi, and aerobic and anaerobic enteric gram-negative rods. The clinical outcome without antibiotic treatment is universally fatal, and even with aggressive treatment, mortality remains around 50%.[5,7] The treatment of bacterial splenic abscess requires drainage, regardless of the inciting organism.[7,8] In cases of a single abscess, percutaneous drainage has been successful in 68% of patients.[8] In a patient with multiple abscesses, splenectomy is recommended.[7,8]

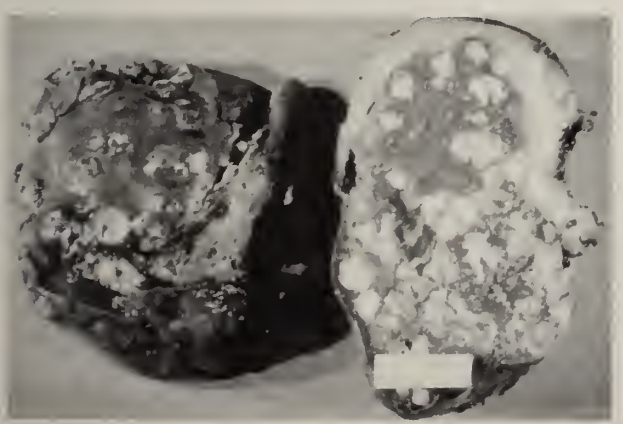


Figure 2.—This pathologic specimen of spleen reveals multiple 1-cm nodules filled with necrotic tissue and organizing macrophages, replacing most of the splenic parenchyma.

This patient was an otherwise healthy woman with diet-controlled non–insulin-dependent diabetes mellitus as her only risk factor for the infection with *Y pseudotuberculosis* and the formation of splenic abscess. She presented with nonspecific symptoms of a generalized illness without abdominal pain or splenomegaly on clinical examination. The only clues on admission that led to an evaluation of her spleen were the abnormal findings on chest roentgenogram and elevated aminotransferase levels. Both of these findings are sensitive for splenic abscess but are nonspecific.[9] Because the organism grows best at lower temperatures, the blood cultures were negative until almost a week into her hospital stay.

An extensive review of the literature suggests that this is the first reported case of *Y pseudotuberculosis* bacteremia and splenic abscess in a diabetic patient. Diabetes is a commonly encountered condition that predisposes to both infection with unusual organisms like *Y pseudotuberculosis* and the development of abscesses. This case emphasizes the potential for occult abscess in diabetic patients and the unusual spectrum of infectious agents to which they are susceptible.

Acknowledgment

We thank Lawrence Crapo, MD, Tom Kelsey, MD, Robert Archibald, MD, John Hamilton, MD, and Ramona Desai, MD, for their support and advice in the production of this report.

REFERENCES

1. Mandell GL, Douglas RG Jr, Bennett JE (Eds). Principles and Practice of Infectious Diseases. New York: Churchill Livingstone, 1990, pp 1754–1755

2. Ljungberg P, Valtonen M, Harjola VP, Kaukoranta-Tolvanen SS, Vaara M. Report of four cases of *Yersinia pseudotuberculosis* septicemia and a literature review. Eur J Clin Microbiol Infect Dis 1995; 14:804–810

3. Farrer W, Kloser P, Ketyer S. *Yersinia pseudotuberculosis* sepsis presenting as multiple liver abscesses. Am J Med Sci 1988; 295:129–132

4. von Graevenitz A, Hany A, Wertheimer Y, Wust J, Zwicky P. *Yersinia pseudotuberculosis*: Unusual features of a case. Infection 1983; 11:208–209

5. Nelken N, Ignatius J, Skinner M, Christensen N. Changing clinical spectrum of splenic abscess. Am J Surg 1987; 154:27–34

6. Paris S, Weiss SM, Ayers WH Jr, Clarke LE. Splenic abscess. Am Surg 1994; 60:358–361

7. Allan JD. Splenic abscess: pathogenesis, clinical features, diagnosis, and treatment. Curr Clin Top Infect Dis 1994; 14:23–51

8. Faught WE, Gilbertson JJ, Nelson EW. Splenic abscess: presentation, treatment options, and results. Am J Surg 1989; 158:612–614

9. Liang JT, Lee PH, Wang SM, Chang KJ. Splenic abscess: a diagnostic pitfall in the ED. Am J Emerg Med 1995; 13:337–343

High-Dose Praziquantel With Cimetidine for Refractory Neurocysticercosis: A Case Report With Clinical and MRI Follow-Up

THOMAS YEE, DO
Stanford, California
JEROME A. BARAKOS, MD
San Francisco, California
ROBERT T. KNIGHT, MD
Davis, California

NEUROCYSTICERCOSIS is an infection of the central nervous system by the larval forms, or cysticerci, of *Taenia solium*, the pork tapeworm,[1] which is prevalent primarily in the rural areas of Latin America, Asia, and Africa.[2–5] The number of cases of neurocysticercosis diagnosed in the United States is rising as a result of the increasing number of immigrants from endemic areas.[6]

There is debate regarding the efficacy of antihelminthic agents in the treatment of neurocysticercosis,[7–8] because the condition may spontaneously resolve without antihelminthic therapy.[9–10] Most clinicians, however, recommend treating active neurocysticercosis with antihelminthic agents,[11–16] using either praziquantel (50 mg/kg/d)[15–21] or albendazole (15 mg/kg/d).[1,15,18,22–24] Praziquantel was the first agent used in the United States and is usually the first drug prescribed for this condition. If a patient does not respond to praziquantel, either a repeat course of praziquantel[17,25] or a trial of albendazole[1,15,18,22–24] is recommended. No consensus has been reached, however, as to the next course of treatment for patients unresponsive to the standard regimens of praziquantel and albendazole.

Several case reports [25] suggest the use of high-dose praziquantel (100 mg/kg/d) in treating refractory neurocysticercosis. We report a case of neurocysticercosis in which a patient failed to respond to conventional treatments but improved after treatment with high-dose praziquantel. This improvement was assessed during follow-up, using clinical observation, brain magnetic resonance imaging (MRI), and cerebrospinal fluid (CSF) studies.

Report of a Case

A 36-year-old Hispanic man presented in 1990 with a headache secondary to neurocysticercosis. Brain MRI revealed multiple parenchymal cysts and calcifications, and CSF studies demonstrated findings consistent with neurocysticercosis. The patient was treated with praziquantel (50 mg/kg/d) and corticosteroids for 15 days, which resulted in the subsequent resolution of his headache. Three months after treatment, a repeat brain MRI showed a reduction in the size of the parenchymal cysts.

In 1993, the patient had a recurrence of headache with diplopia and vertigo. A brain MRI revealed new parenchymal cystic lesions, and CSF studies, using the enzyme-link immunosorbent assay, detected the presence of anticysticercal antibodies. The patient was again treated with praziquantel (50 mg/kg/d), this time without corticosteroids, for 21 days. His symptoms, however, persisted three months after treatment. A repeat brain MRI did not reveal a significant reduction in the size of the parenchymal cystic lesions, and communicating hydrocephalus was now found. A ventriculoperitoneal shunt was placed, and some of the patient's symptoms subsequently improved, although his headache persisted. One year later, a follow-up brain scan showed new parenchymal cystic lesions with normal-sized ventricles. As a result, he was placed on a 30-day regimen of albendazole (15 mg/kg/d) without corticosteroids. This treatment was discontinued after 28 days, owing to a sudden onset of left hemiparesis and hemianesthesia associated with slurred speech and dysphagia. The patient was subsequently started on dexamethasone (12 mg/d), and these symptoms improved gradually over 4 to 7 days. A brain MRI revealed new parenchymal cystic lesions, hydrocephalus, an increase in basilar leptomeningeal disease, and evidence of subcortical infarcts in the lenticulostriate arterial distribution (Figures 1 and 2).

(Yee T, Barakos JA, Knight RT. High-dose praziquantel with cimetidine for refractory neurocysticercosis: a case report with clinical and MRI follow-up. West J Med 1999; 170:112–115)

From the VA Palo Alto Health Care System, Palo Alto, California, and the Department of Neurology and Neurological Sciences, Stanford University, School of Medicine, Stanford, California (Dr Yee); the Department of Radiology, California Pacific Medical Center and the University of California, San Francisco, California (Dr Barakos); and the VA Northern California Health Care System, Martinez, California, and the Department of Neurology, University of California-Davis, Davis, California (Dr Knight).

Reprint requests to Dr. Thomas Yee, VA Palo Alto Health Care System, Neurology Service (127), 3801 Miranda Avenue, Palo Alto, CA 94304.

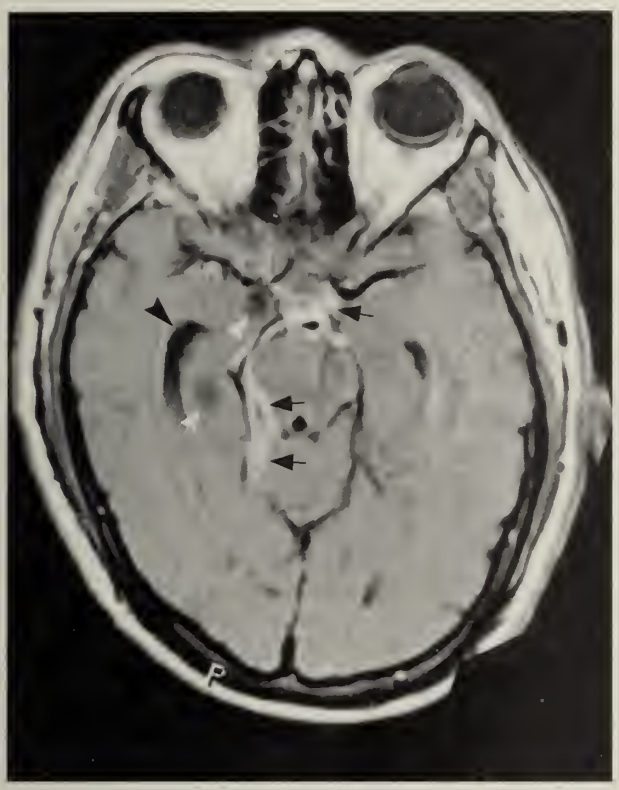


Figure 1.—Post-contrast enhanced T1-weighted images (TR = 500, TE = 30 mseconds) taken prior to high-dose praziquantel treatment reveal mild hydrocephalus evidenced by enlargement of the temporal horn (arrowhead). Extensive leptomeningeal enhancement is noted within the basilar cisterns (black arrows). Two intraparenchymal cysts are evident in the right mesial temporal region (white arrows).

Figure 2.—Post-contrast enhanced T1-weighted images (TR = 500, TE = 30 mseconds) obtained one day after the onset of stroke symptoms reveal two contrast enhancing lesions within the right corpus striatum. These lesions are secondary to ischemia in the territory of the lenticulostriate branches.

Three months after albendazole treatment, such symptoms as headache, mild dysphagia and left-hand weakness persisted. A repeat brain MRI revealed minimal change in the parenchymal cystic lesions and basilar leptomeningeal disease. The patient was started on a 21-day regimen of high-dose praziquantel (100 mg/kg/d) with aspirin (325 mg/d), cimetidine (800 mg/d), and dexamethasone (12 mg/d). Dexamethasone was tapered off over 2 months. The patient tolerated the treatment well, without any complications. Three months after treatment, his headache had improved greatly. A brain MRI showed that both the mesial temporal parenchymal cystic lesions and basilar leptomeningeal disease had improved. CSF studies demonstrated an increased glucose level, a decreased protein level, and a lowered white blood cell count after high-dose praziquantel treatment (Table 1).

TABLE 1.—*Cerebrospinal Fluid Profile Before and After High-Dose Praziquantel Treatment*

Time	*Glucose (45–80 mg/dl)*	*Protein (15–45 mg/dl)*	*WBC (<6 mm³)*
Three days before treatment	47	143	62
Five days after treatment	53	115	40
Three months after treatment	57	87	48

WBC = white blood cell

At follow-up, 18 months after treatment, the patient continued to do well clinically. A brain MRI demonstrated further improvement in the parenchymal cystic lesions and a marked reduction in the basilar leptomeningeal disease (Figure 3).

Discussion

Praziquantel is generally the first agent employed in the treatment of neurocysticercosis, with dosages varying from 5 to 75 mg/kg/d.[26,27] Most authorities[1,11,13,21,27–33] recommend a dose of 50 mg/kg/d for 15 or 21 days. If a patient fails to respond to an initial course of praziquantel, the literature suggests either a repeat course[17,25] or a trial of albendazole at 15 mg/kg/d for 8 or 30 days.[1,15,18,22–24] Albendazole has proven as effective as, if not superior to, praziquantel in the treatment of neurocysticercosis.[14,18,20,34,35] There is very little data in the literature, however, indicating the next course of treatment for refractory neurocysticercosis in the event that these standard treatments fail.

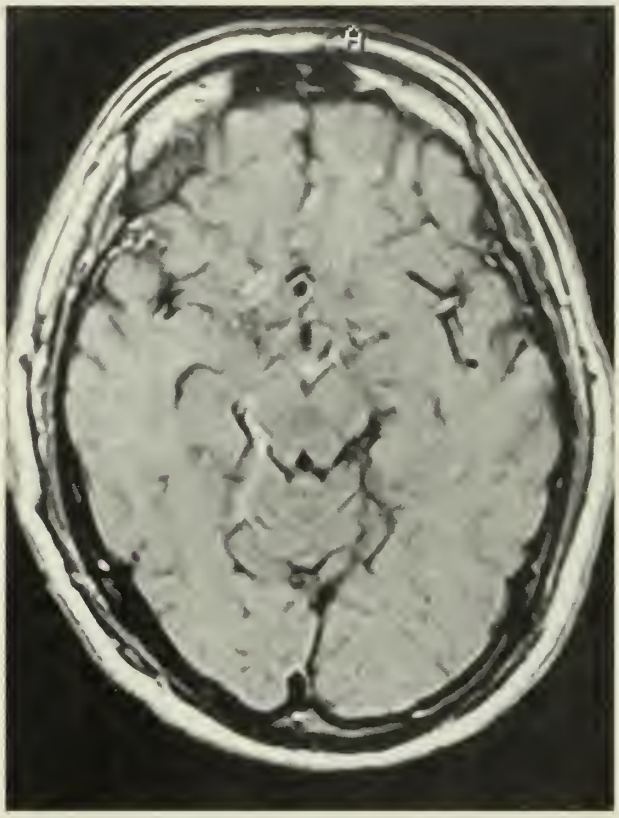


Figure 3.—Post-contrast enhanced T1-weighted images (TR=500, TE=30 mseconds) taken after high-dose praziquantel treatment reveal considerable reduction in the extent of leptomeningeal disease within the basilar cisterns. Hydrocephalus and intraparenchymal cysts have resolved.

Although our patient is a resident of California, he had traveled to the rural areas of Mexico in the past. His travel history after his initial treatment for neurocysticercosis in 1990 was unclear. The stool specimens of both the patient and his family members tested negative for tapeworm infection. Thus, the patient's recurrence of neurocysticercosis could have resulted from repeated visits to an endemic area. Recurrent neurocysticercosis has been observed, however, in patients without any travel history to endemic areas,[17] which suggests that there may be sequestration of the larval forms in an unidentified location. During his recurrence of neurocysticercosis, the patient failed to respond to either a repeat course of standard praziquantel therapy or an additional course of albendazole. In addition, he had a lacunar stroke involving the territory of the lenticulostriate branches during one of these antihelminthic treatments (Figure 2).

Ischemic cerebrovascular disease has been reported as a complication in untreated neurocysticercosis patients and in patients receiving anticysticercal drugs.[36–39] In most cases, the stroke involves vessels of small diameter in the territory of the lenticulostriate branches of the anterior or middle cerebral artery and results in a lacunar syndrome.[36] A cerebral infarct is caused by occlusive endarteritis secondary to the intense inflammatory reaction triggered within the subarachnoid space by meningeal cysticerci.[36] Anticysticercal drugs may enhance the inflammatory reaction and increase the likelihood of cerebral infarcts.[36,37] Because the patient's stroke during antihelminthic treatment was likely the result of an inflammatory arterial occlusion, he was given dexamethasone, in addition to praziquantel, during the high-dose praziquantel treatment. Furthermore, because plasma levels of praziquantel decrease with concomitant dexamethasone treatment,[40] cimetidine, which has been reported to increase the bioavailability of praziquantel, most likely by inhibiting cytochrome P-450 hepatic metabolism, was also included in the regimen.[41] Although praziquantel concentrations were not measured in our patient, cimetidine may have played an important role in the success of his treatment by minimizing the variations in plasma concentration that result from extensive first pass metabolism of praziquantel.[41] The regimen of high-dose praziquantel, dexamethasone, and cimetidine was well tolerated.

Three months after high-dose praziquantel treatment, a repeat brain MRI showed improvement in the parenchymal cystic lesions and leptomeningeal disease. A follow-up brain MRI at 18 months demonstrated continuing resolution of the parenchymal cysts and a marked reduction of the basilar leptomeningeal disease (Figure 3). Spinal fluid findings also provided evidence of improvement three months after the patient's treatment with high-dose praziquantel (Table 1). It is unlikely that the improvements evidenced by the brain MRI resulted from prior albendazole treatment. Previous reports have found that in most neurocysticercosis patients who respond to albendazole, lesions disappear on brain MRIs within three to four weeks.[42,43] In this case, the patient's lesions persisted three months after albendazole therapy.

In a report by Bittencourt and colleagues,[25] three patients with neurocysticercosis who had previously failed to respond to a standard regimen of praziquantel were subsequently treated with high-dose praziquantel. Although two of these patients died from recurrent shunt complications at 18- and 21-month follow-ups, all three improved initially upon treatment with high-dose praziquantel. Like our patient, they all tolerated high-dose praziquantel. Taken together, the results of Bittencourt and colleagues' study and the case we are presenting suggest that high-dose praziquantel may be a safe and effective treatment for patients with refractory neurocysticercosis who do not respond to standard regimens of either praziquantel or albendazole. Because the use of antihelminthic agents may lead to cerebral infarction subsequent to angiitis caused by acute inflammatory reaction,[37–39] the addition of dexamethasone, with or without cimetidine, may help decrease the risk of untoward vascular events during high-dose praziquantel therapy.

REFERENCES

1. Del Brutto OH, Sotelo J. Neurocysticercosis: an update. Rev Infect Dis 1988; 10:1075–1087

2. Nash TE, Neva FA. Recent advances in the diagnosis and treatment of cerebral cysticercosis. N Engl J Med 1984; 311:1492–1496

3. Gemmell M, Matyas Z, Pawlowski Z, Soulsby EJL (Eds). Guidelines for Surveillance, Prevention, and Control of Taeniasis/Cysticercosis. Geneva, Switzerland, World Health Organization publication No. (VPH) 83–49, 1983

4. World Health Organization (WHO). Prevention and control of intestinal parasitic infections: report of a WHO expert committee. World Health Organ Tech Rep Ser 1987; 749:1–86

5. Mahajan RC. Geographical distribution of human cysticercosis, In Flisser A, Willms K, Laclette JP, et al (Eds). Cysticercosis: Present State of Knowledge and Perspectives. New York, NY, Academic Press, 1982, pp 39–46

6. 1990 Census Profile: Race and Hispanic Origin. No. 2. Washington, DC, Department of Commerce, 1991, pp 1–7

7. Carpio A, Santillán F, León P, et al. Is the course of neurocysticercosis modified by treatment with antihelminthic agents? Arch Intern Med 1995; 155:1982–1988

8. Kramer D. Medical treatment of cysticercosis-ineffective. Arch Neurol 1995; 52:101–102

9. Miller B, Grinnell V, Goldberg MA, Heiner D. Spontaneous radiographic disappearance of cerebral cysticercosis: three cases. Neurology 1983; 33:1377–1379

10. Kramer LD, Locke GE, Byrd SE, Daryabagi J. Cerebral cysticercosis: documentation of natural history with CT. Radiology 1989; 171:459–462

11. Del Brutto OH. Medical treatment of cysticercosis-effective. Arch Neurol 1995; 52:102–104

12. Sotelo J, Torres B, Rubio-Donnadieu F, et al. Praziquantel in the treatment of neurocysticercosis: long-term follow-up. Neurology 1985; 35:752–755

13. Robles C, Sedano AM, Vargas-Tentori N, et al. Long-term results of praziquantel therapy in neurocysticercosis. J Neurosurg 1987; 66:359–363

14. Takayanagui OM, Jardim E. Therapy for neurocysticercosis: comparison between albendazole and praziquantel. Arch Neurol 1992; 49:290–294

15. Barry M, Kaldjian LC. Neurocysticercosis. Semin Neurol 1993; 13:131–143

16. Sotelo J. Cerebral cysticercosis. In Johnson RT, Griffin JW (Eds). Current Therapy in Neurologic Disease. 5th ed. St. Louis, Mo, Mosby, 1997, pp 131–135

17. Shandera WX, White AC, Chen JC, et al. Neurocysticercosis in Houston, Texas: a report of 112 cases. Medicine 1994; 73:37–52

18. Sotelo J, Escobedo F, Penagos P. Albendazole versus praziquantel for therapy for neurocysticercosis: a controlled trial. Arch Neurol 1988; 45:532–534

19. Vasconcelos D, Cruz-Segura H, Mateos-Gomez H, Alanis GZ. Selective indications for the use of praziquantel in the treatment of brain cysticercosis. J Neurol Neurosurg Psy 1987; 50:383–388

20. Vazquez V, Sotelo J. The course of seizures after treatment for cerebral cysticercosis. N Engl J Med 1992; 327:696–701

21. Sotelo J, Escobedo F, Rodriguez-Carbajal J, et al. Therapy of parenchymal cysticercosis with praziquantel. N Engl J Med 1984; 310:1001–1007

22. Sotelo J, Penagos P, Escobedo F, Del Brutto OH. Short course of albendazole therapy for neurocysticercosis. Arch Neurol 1988; 45:1130–1133

23. Escobedo F, Sotelo J, Penagos P, Rodriguez J, Del Brutto OH. Albendazole therapy for human neurocysticercosis: a controlled trial with computerized tomography and magnetic resonance imaging. Acta Leidensia 1989; 57:247–254

24. Carpio A, Santillán F, León P, Borrero A, Tinoco L. New treatment of brain cysticercosis with albendazole [abstract]. Ann Neurol 1988; 24:144

25. Bittencourt PRM, Gracia CM, Gorz AM, et al. High-dose praziquantel for neurocysticercosis: efficacy and tolerability. Eur Neurol 1990; 30:229–234

26. Groll EW. Chemotherapy of human cysticercosis with praziquantel, In Flisser A, Willms K, Laclette JP, et al (Eds): Cysticercosis: Present State of Knowledge and Perspectives. New York, NY, Academic Press, 1982, pp 207–218

27. Bittencourt PRM, Gracia CM, Lorenzana P. Epilepsy and parasitosis of the central nervous system, In Pedley TA, and Meldrum MS (Eds). Recent Advances in Epilepsy. Vol 4. Edinburgh, Scottland, Churchill Livingstone, 1988, pp 123–159

28. Cook GC. Neurocysticercosis: parasitology, clinical presentation, diagnosis, and recent advances in management. Q J Med 1988; 256:575–583

29. Bittencourt PRM, Gorz AM, Oliveira TV, Mazer S. Neurocysticercosis: conceptos básicos de clínica y tratamiento. Parte II, Acta Neurol Colomb 1986B;3:11–14.

30. Botero D, Cataño S. Treatment of cysticercosis with praziquantel in Colombia. Am J Trop Med Hyg 1982; 31:810–821

31. Leblanc R, Knowles KF, Milanson D, MacLean JD, Roulean G, Farmer JP. Neurocysticercosis: surgical and medical management with praziquantel. Neurosurg 1986; 18:419–427

32. Pearson RD, Guerrant RL. Praziquantel: a major advance in antihelminthic therapy. Ann Intern. Med 1983; 99:195–198

33. Spina-Franca A, Nobrega JPS, Livramento JA, Machado LR. Administration of praziquantel in neurocysticercosis. Tropenmed Parasitol 1982; 33:1–4

34. Cruz M, Cruz I, Horton J. Albendazole versus praziquantel in the treatment of cerebral cysticercosis: clinical evaluation. Trans R Soc Trop Med Hyg 1991; 85:244–247

35. Sotelo J, Del Brutto OH, Penagos P, et al. Comparison of therapeutic regimen of anticysticercal drugs for parenchymal brain cysticercosis. J Neurol 1990; 237:69–72

36. Del Brutto OH. Cysticercosis and cerebrovascular disease: a review. J Neurol Neurosurg Psy 1992; 55:252–254

37. Barinagarrementeria F, Del Brutto OH. Lacunar syndrome due to cysticercosis. Arch Neurol 1989; 46:415–417

38. Del Brutto OH, Sotelo J, Roman GC. Therapy for neurocysticercosis: a reappraisal. Clin Infect Dis 1993; 17:730–735

39. Bang OY, Heo JH, Choi SA, Kim DI. Large cerebral infarction during praziquantel therapy in neurocysticercosis. Stroke 1997; 28:211–213

40. Vazquez ML, Jung H, Sotelo J. Plasma levels of praziquantel decrease when dexamethasone is given simultaneously. Neurology 1987; 37:1561–1562

41. Dachman WD, Adubofour KO, Bikin DS, et al. Cimetidine-induced rise in praziquantel levels in a patient with neurocysticercosis being treated with anticonvulsants. J Infect Dis 1994; 169:689–691

42. Martinez HR, Rangel-Guerra R, Arredondo-Estrada JH, et al. Medical and surgical treatment in neurocysticercosis a magnetic resonance study of 161 cases. J Neurol Sci 1995; 130:25–34

43. Martinez HR, Rangel-Guerra R, Elizondo G, et al. MR imaging in neurocysticercosis: a study of 56 cases. AJNR 1989; 10:1011–1019

Diabetic Ketoacidosis in Pregnancy With a Recent Normal Screening Test

MICHAEL J. O'SHAUGHNESSY, MD
KELLI R. BEINGESSER, MD
WILLIAM U. KHIEU, MD
San Francisco, California

KETOACIDOSIS IS A RARE complication of diabetic pregnancies. It occurred at a rate of 1.73% in a recent series of pregnancies with preexisting, insulin-dependent diabetes.[1] Ketoacidosis is an extremely rare complication of gestational diabetes, as well.[2–3] In addition, ketoacidosis has been reported in two patients with previously undiagnosed diabetes.[3–4] We report a case of early diabetic ketoacidosis involving a patient who had had a normal glucose tolerance test (GTT) only 10 days before presentation.

Case Report

A previously healthy, 23-year-old, gravida II, para I, Asian woman arrived at the obstetrical service in her 36th-week of pregancy, complaining of contractions every three minutes and decreased fetal movement. The patient also admitted to polyuria and polydipsia. She denied nausea, vomiting, fever and chills. She had no signs or symptoms of genitourinary, respiratory, or gastrointestinal infectious processes. Her past medical history was unremarkable. Her past obstetrical history

(O'Shaughnessy MJ, Beingesser KR, Khieu WU. Diabetic ketoacidosis in pregnancy with a recent normal screening test. West J Med 1999; 170:115–118)

From the University Medical Center, University of California, San Francisco Fresno-Central San Joaquin Valley Medical Education Program, Fresno, California.

Reprint requests to Michael J. O'Shaughnessy, MD, University of California, San Francisco Fresno-Central San Joaquin Valley Medical Education Program, 445 South Cedar Avenue, Fresno, CA 93702.

included one prior pregnancy with delivery of malpresenting twins at 38 weeks by cesarean section. During that pregnancy, routine screening for gestational diabetes had been negative. The present pregnancy had also been unremarkable up to this time. At 15 weeks, the patient had had a 50-gram 1-hour glucose challenge test, which was mildly elevated at 149 mg/dl. (Our facility normally screens patients upon presentation, owing to the prevalence of gestational diabetes in the population served and the fact that much of the population is transient.) A follow-up 100-gram 3-hour GTT was normal at 20 weeks, and at 35 weeks, 10 days prior to her admission, the patient had a second 50-gram 1-hour screening test, which was also normal at 106 mg/dl. Physical examination revealed an alert and oriented patient in no distress. Her vital signs included a blood pressure of 107/57, a pulse of 104, a respiratory rate of 18, and a temperature of 37.3°C. Her abdomen was not tender, there were no localizing signs of infection, and fundal height was in agreement with the estimated gestational age. Cervical examination showed the patient to be in early labor with the vertex presenting. Contractions were coming every two to three minutes.

Continuous fetal heart monitoring revealed a baseline of 150 beats per minute with good variability, but with the presence of late decelerations. Ultrasound was remarkable for oligohydramnios.

Initial laboratory investigations included a urinalysis remarkable for severe glucosuria and ketonuria, a serum sodium level of 129 mM, a potassium level of 5.2 mM, and a serum glucose level of 593 mg/dl with an elevated anion gap of 18 mmol/liter.

Based on this initial data, diabetic ketoacidosis was suspected. Arterial blood gases revealed a pH of 7.32, a PCO^2 of 28 mm Hg, a bicarbonate level of 14.2 mM, and a base excess of –10. Blood counts included a leukocyte count of 13,700/mm^3 and a hematocrit of 35.7%. Serum ketones were present, and the patient had a lactic acid level of 2.7 mmol/liter (normal range: 0.6–1.7 mmol/liter); a glycosylated hemoglobin level of 7.1% (normal range 5.0–7.3%); and a fructosamine of 232 mmol/liter (normal range 0–285 mmol/liter).

Treatment consisted of volume expansion, correction of hyperglycemia, replacement of sodium and potassium, and oxygen therapy. The volume deficit was addressed with a rapid infusion of isotonic saline (1.5 liters in the first hour). We teated the hyperglycemia with an intravenous insulin drip. As the serum glucose approached 200 mg/dl, we added 5% dextrose to the infusion. We began potassium replacement two to three hours after we initiated therapy. Twelve hours after the initial therapy, the patient's blood glucose level reached 181 mg/dl, and the serum ketones were negative. During this initial phase of treatment, insulin was given as a one-time, 12-unit bolus of regular insulin, followed by a continuous, intravenous drip of 5 to 6 units per hour.

At 16 hours, the patient underwent a vacuum-assisted, vaginal delivery. Apgar scores climbed from eight at one minute to nine at five minutes. Maternal arterial pH was 7.41 at delivery. Serum glucose was 160 mg/dl. It is of note that the fetal late decelerations resolved promptly with volume replacement, oxygen therapy, and left lateral positioning.

In the immediate postpartum period, the patient regained good glycemic control with relatively modest doses of insulin (10 units of regular, 10 units of NPH per day). Three months after discharge, the patient was readmitted with a second episode of diabetic ketoacidosis. On admission, she had a serum glucose level of 534 mg/dl. This episode was felt to be due to increasing insulin requirements and poor compliance. After this hospitalization, the patient became pregnant again. This pregnancy has been complicated by increasing insulin requirements. The patient has been admitted to the hospital on several occasions for hyperglycemia and has also experienced severe symptomatic episodes of hypoglycemia. There have been no episodes of ketoacidosis in this most recent pregnancy.

Discussion

In rare instances, diabetes mellitus can present initially as diabetic ketoacidosis during pregnancy. In the case we are discussing, the patient had had a screening test for gestational diabetes with normal results only 10 days prior to her admission for ketoacidosis. Laboratory records reflect proper administration of the glucose load and make no mention of any emesis during the testing period. This, however, does not rule out the possiblity of laboratory error or poor patient compliance with the test protocol.

As we mentioned previously, our facility normally screens for diabetes upon presentation for prenatal care. This patient's abnormal screening at the early gestational age of 15 weeks is interesting, but of uncertain significance. The 100-gram 3-hour GTT, however, is the diagnostic test for gestational diabetes, and the patient's test was normal.

A normal glycosylated hemoglobin level and fructosamine show that the patient had not had any significant disturbances in glucose metabolism during the months prior to presentation. This may represent a case of pancreatic islet-cell failure of relatively acute onset. Rapid depletion of insulin, coupled with the stress of labor, precipitated diabetic ketoacidosis. A brief review of the genesis of diabetic ketoacidosis, the effects of pregnancy on the disease process, and the disease's effects on the fetus follows.

Diabetic ketoacidosis is a state of relative or absolute lack of insulin, which leads to major changes in metabolic pathways.[5] A lack of insulin seriously impairs the body's ability to use glucose as a peripheral energy source. The organism must continue to produce glucose in order to support brain function, but must also provide an alternative energy source for peripheral use. Protein catabolism provides a substrate for hepatic gluconeogenesis, which supports central nervous system function, but, unfortunately, also contributes to the overall state of hyperglycemia.[6] Hyperglycemia in turn

helps to stimulate increasing lipolysis with the release of free fatty acids. Oxidation of free fatty acids in the liver produces ketonemia and, eventually, metabolic acidosis.[7] Hyperglycemia also results in glucosuria and osmotic diuresis. Free water and electrolytes are lost in the urine, leading to dehydration and electrolyte imbalances. Water shifts from the intracellular space to replenish the intravascular volume, and, eventually, with continued diuresis, all body compartments can become dehydrated. Serum hyperosmolarity results in the increased secretion of counter-regulatory hormones, such as glucagon, catecholamines, growth hormone and cortisol.[5] These hormones, in turn, contribute to the overall state of hyperglycemia and increase the maladaptive attempt to use large amounts of free fatty acids as an energy source.[7]

Pregnancy in particular can predispose a patient to ketoacidosis in several ways. In the fasting state, the increased use of glucose by both the fetal and maternal units can lead relatively quickly to conversion to a catabolic metabolism.[8] This condition of accelerated starvation is further characterized by hypoinsulinemia, hypoglycemia and, more importantly, hyperketonemia and protein catabolism.[9] Pregnancy-associated nausea and vomiting can contribute as well.

Relative respiratory alkalosis associated with increased alveolar minute-ventilation causes a compensatory increase in renal bicarbonate excretion. As a consequence, a deficit in buffering capacity develops, which becomes especially important in the presence of an acid load, as is the case in ketonemia.[10]

The production of diabetogenic hormones, such as human placental lactogen, prolactin and cortisol, increases over the course of gestation, thereby predisposing the patient to ketoacidosis.[11]

During pregnancy, miscellaneous conditions, such as infection, beta-sympathomimetic therapy, and labor can increase endogenous catecholamine release, thereby contributing to the onset of diabetic ketoacidosis.[10]

As we discussed earlier, metabolic, acid-base, and hormonal conditions normal to pregnancy can predispose the diabetic patient to ketoacidosis. In addition, it has been demonstrated that, during pregnancy, diabetic ketoacidosis can occur at glucose levels as low as 200 mg/dl.[12]

The precise effects of diabetic ketoacidosis on the fetus are unknown, although abnormal heart-rate patterns consistent with fetal acidosis have been reported.[13] In severe cases of ketoacidosis, especially those associated with maternal coma, fetal demise is common.[14] Most series report good outcomes for the fetus, if it is alive upon presentation to the hospital and prompt, appropriate, maternal interventions are initiated.[15] We cannot overemphasize the importance of continuous fetal heart-rate monitoring in this setting.

In cases of maternal diabetic ketoacidosis, a number of factors most likely contribute to the development of fetal acidosis. Maternal hypovolemia and catecholamine excess may result in decreased, uterine blood flow.[5] Fetal hyperinsulinemia, resulting from hyperglycemic conditions, will increase fetal oxygen demands.[16] Maternal phosphate deficiency may deplete erythrocytes of 2,3-diphosphoglycerate, thereby impairing oxygen delivery to the fetus.[5] Hyperglycemia has been shown to decrease myocardial contractility in animal models.[17] Finally, maternal metabolic acidosis and electrolyte disturbances will be directly reflected in the fetal compartment. For example, fetal cardiac arrest has been reported in connection with severe, maternal hypokalemia.[12]

In our case, the patient presented with late decelerations and oligohydramnios. These findings were probably manifestations of uteroplacental insufficiency, secondary to maternal dehydration and metabolic acidosis. Correction of maternal fluid deficits and acidosis resulted in the normalization of the fetal heart-rate pattern.

The genesis of rapid-onset, islet-cell failure and resultant diabetes remains a controversial topic. Research suggests, however, that the genesis may be related to recent viral infection.[18] Considerable animal data link diabetes with particular strains of common viruses.[19] The data on humans, however, is less certain. We do not know whether pancreatic viral infection would result in transient or permanent pathology.[19] In several studies, evidence of viral infection in the peripheral blood or pancreatic tissue was found no more commonly in insulin-dependent, diabetic patients than in non-diabetic individuals.[20,21] This finding, however, may reflect either the elimination of the diabetogenic viruses by the time of diagnosis or their behavior as nonspecific agents to which the host has an abnormal immune response.[21] Indeed, viruses may induce changes in cell proteins, which the immune system subsequently identifies as foreign.[22,23]

There is some evidence that susceptibility to the diabetogenic effects of viruses may be genetic.[22] Certain viral strains seem to be more tropic for beta cells than others.[18] Furthermore, in rare instances, toxins, such as lead, have been implicated in rapid-onset diabetes.[22]

We could obtain no clear history of antecedent viral infection or toxin exposure for the patient under discussion. A subclinical or minimally symptomatic infection could have been present. We should emphasize that the association of acute islet-cell failure with recent viral infection in humans remains purely theoretical. Furthermore, in the present case, titers for islet-cell antibodies or for antibodies to suspected diabetogenic viruses were, unfortunately, not obtained at the time of presentation. Although not critical to the management of this patient, this information may have added to our understanding of this case.

The patient's course, since the index pregnancy, has been notable for waxing and waning pancreatic function with corresponding wide swings in glycemic control. Since the initial presentation, she has continued to require insulin, as is clearly evidenced by a hospital admission for diabetic ketoacidosis three to four weeks postpartum and by admissions for poorly controlled diabetes early in a subsequent pregnancy.

It is of note that the patient's diabetes was easily controlled in the immediate postpartum period with low doses of insulin. This "honeymoon period" of improved glycemic status following delivery of the fetus and placenta results from falling levels of diabetogenic hormones, particularly human placental lactogen. In the typical insulin-dependent diabetic individual, insulin requirements will usually increase to prepregnancy levels within four to six days after delivery.[24] We do not know, however, what the pregnant, newly diagnosed, diabetic patient's true insulin requirements will be after delivery. We believe that failure to recognize increasing insulin requirements in the weeks following delivery may have contributed to this patient's postpartum episode of ketoacidosis.

In summary, diabetic ketoacidosis can be managed successfully during pregnancy, if certain basic principles are kept in mind. Volume deficits must be quickly corrected in order to improve tissue perfusion and dilute plasma glucose concentrations.[24] Hyperglycemia must be treated with insulin replacement. Once plasma glucose levels are clearly falling, carbohydrates should be provided to the patient via intravenous infusion in order to insure normal cellular metabolism.[24] Electrolyte disturbances must be corrected. Serum potassium levels may be normal or mildly elevated on presentation, but intracellular levels may be low. Upon correction of the acidosis and institution of insulin therapy, the intracellular influx of potassium will result in falling serum levels. Finally, the search for and correction of precipitating factors, such as infection, emesis, and beta-agonist use, should be undertaken.

Sudden islet-cell failure can occur in pregnancy with the acute onset of hyperglycemia and diabetic ketoacidosis. Certain viruses may be direct or indirect precipitants of this disorder, although we lack conclusive evidence of this in humans.

REFERENCES

1. Kilvert JA, Nicholson HO, Wright AD. Ketoacidosis in diabetic pregnancy. Diabetic Med 1993; 10:278–281

2. Maislos M, Harman-Bohem I, Weitzman S. Diabetic ketoacidosis: a rare complication of gestational diabetes. Diabetic Care 1992; 15:968–970

3. Clark JDA, McConnell A, Hartog M. Normoglycemic ketoacidosis in a woman with gestational diabetes. Diabetic Med 1991; 8:388–389

4. Abourizk NN. Diabetic ketoacidosis in pregnancy: another atypical case [letter]. Diabetes Care 1993; 16:661–662

5. Hagay ZG. Diabetic ketoacidosis in pregnancy: Etiology, pathophysiology, and management. Clin Obstet Gynecol 1994; 37:39–49

6. Kitabachi A. Low-dose insulin therapy in DKA: fact or fiction? Diabetes Metab Rev 1989; 5:337–369

7. Hagay Z, Reece EA. Diabetes mellitus in pregnancy. In Reece EA, Hobbins JC, Mahoney, Petrie RH (Eds). Medicine of the Fetus and the Mother. Philadelphia, Pa, JB Lippincott, 1992, pp 982–1020

8. Metzger BE, Freinkel N. Effects of diabetes mellitus on endocrinologic and metabolic adaptations of gestation. Semin Perinatol 1978; 2:309–315

9. Metzger BE, Vilesis RA, Ravnikar V, et al. "Accelerated starvation" and the skipped breakfast in late normal pregnancy. Lancet 1982; 1:588–592

10. Chauhan SP, Perry KG. Management of diabetic ketoacidosis in the obstetric patient. Obstet Gynecol Clin North Am 1995; 22:143–155

11. Kallkhoff RK, Kissebah AH, Kim HJ. Carbohydrate and lipid metabolism during normal pregnancy: Relationship to gestational hormone action. Semin Perinatol 1978; 2:291–294

12. Kitzmiller JL. Diabetic ketoacidosis and pregnancy. Contemp Obstet Gynecol 1982; 20:141

13. Rhodes RW, Ogburn PL. Treatment of severe DKA in the early third trimester in a patient with fetal distress. J Reprod Med 1984; 299:621–624

14. Kyle GC. Diabetes and pregnancy. Ann Intern Med 1963; 10:17–20

15. Montoro MN, Myers VP, Mestman, et al. Outcome of pregnancy in DKA. Am J Perinat 1993; 10:17–20

16. Philipps AF, Rosenkrantz TS, Raye J. Consequences of perturbations of fetal fuels in ovine pregnancy. Diabetes 1985; 54:32

17. Bard H, Fouron JC, Demuylder X, et al. Myocardial function and hemoglobin oxygen affinity during hyperglycemia in the fetal lamb. J Clin Invest 1986; 78:191

18. Szopa TM, Titchener PA, Portwood ND, Taylor KW. Diabetes mellitus due to viruses: Some recent developments. Diabetologia 1993; 36:687–695

19. See DM, Tilles JG. Pathogenesis of virus-induced diabetes in mice. J Infect Dis 1995; 171:1131–1138

20. Foy CA, Quirke P, Williams DJ, et al. A search for candidate viruses in type 1 diabetic pancreas using the polymerase chain reaction. Diabetic Med 1994; 11:564–569

21. Foy CA, Quirke P, Lewis FA, Futers TS, Bodansky HJ. Detection of common viruses using the polymerase chain reaction to assess levels of viral presence in type 1 (insulin-dependent) diabetic patients. Diabetic Med 1995; 12:1002–1008

22. Berdanier CB. Diet, autoimmunity, and insulin-dependent diabetes mellitus: a controversy. Proc Soc Exp Biol Med 1995; 209:223–230

23. von Herrath MG, Dockter J, Oldstone MBA. How virus induces a rapid or slow onset insulin-dependent diabetes mellitus in a transgenic model. Immunity 1994; 1:231–242

24. Golde SH. Diabetic ketoacidosis in pregnancy. In Clark SL, Cotton DB, Hankins GDV, Phelan JP (Eds). Critical Care Obstetrics. Cambridge, Mass, Blackwell Scientific Publications, 1991, pp 329–339

Parathyroid Cyst: An Uncommon Cause of a Palpable Neck Mass and Hypercalcemia

SEAN P. PINNEY, MD
PATRICIA A. DALY, MD
Boston, Massachusetts

PARATHYROID CYSTS ARE rare lesions arising in the neck and anterior mediastinum. Goris[1] reported the first case in 1905, and since then, fewer than 250 cases have been published in the literature. Parathyroid cysts constitute only 0.6% of all thyroid and parathyroid lesions,[2] but should be considered in the differential diagnosis of anterior neck masses, particularly in the presence of hypercalcemia.

(Pinney SP, Daly PA. Parathyroid cyst: an uncommon cause of a palpable neck mass and hypercalcemia. West J Med 1999; 170:118–120)

From the Department of Internal Medicine (Dr Pinney), Beth Israel Deaconess Medical Center - West Campus, and the Division of Endocrinology and Metabolism (Dr Daly), Beth Israel Deaconess Medical Center, Boston, Massachusetts.

Reprint requests to Patricia A. Daly, MD, Division of Endocrinology and Metabolism, Beth Israel Deaconess Medical Center, 110 Francis Street, Suite 9D, Boston, MA 02215.

Report of a Case

A 66-year-old man was referred to endocrinology for evaluation of a neck mass. For four years he had been followed by his primary care physician for hypercalcemia attributed to primary hyperparathyroidism with serum calcium concentrations as high as 3.1 mmol per liter (12.5 mg per dl; normal, 2.1–2.6 mmol per liter). The patient denied fatigue, polyuria, or history of peptic ulcers. During doppler ultrasonography of his carotid arteries, a complex 1.5 × 1.5 cm cystic mass was incidentally discovered in the left lower pole of the thyroid. Subsequent technetium 99 scanning showed homogeneously decreased tracer accumulation in the left lobe without evidence of focal hot or cold areas. He was then referred to us. On physical examination, he appeared well and was normotensive. A 1-cm flat nodule was palpable at the lateral aspect of the lower pole of his thyroid. Laboratory studies yielded the following results: calcium, 3.0 mmol per liter; phosphorous, 1.07 μmol per liter (3.3 mg per dl; normal, 0.81–1.65 μmol per liter); creatinine, 159 mmol per liter (1.8 mg per dl; normal, 44–115 mmol per liter); intact parathyroid hormone (hPTH), 112 ng per liter (normal, 10–65); thyroid-stimulating hormone (TSH), 1.93 mIU/ml (normal, 0.23–4.00). A 24-hour urine calcium totaled 11.8 mmol (471 mg; normal 0.0–7.5 mmol). Fine needle aspiration (FNA) of the cyst was performed under ultrasound guidance, and 8 ml of amber, blood-streaked fluid was removed. The fluid's intact hPTH level was 163,000 ng per liter. Cytological examination revealed hemosiderin-laden macrophages and a few, benign-appearing, follicular cells that did not stain for thyroglobulin. Two days after the FNA, the patient complained of fatigue and polyuria. The serum calcium level had risen to 3.3 mmol per liter, but fell to 3.0 mmol per liter over 72 hours with aggressive oral fluid intake and furosemide. One month after the FNA, his mass was surgically removed and found to be a parathyroid cyst arising from a degenerating parathyroid adenoma. Both his serum calcium and creatinine returned to normal, and his fatigue resolved.

Discussion

Prior to the advent of fine needle aspiration, nearly all parathyroid cysts were diagnosed surgically. Most patients presented with either a mass or with symptoms arising from compression caused by a mass. In 1953, Crile[3] reported the first case diagnosed preoperatively using FNA. Since then, the literature has focused on two broad categories of parathyroid cysts: functioning and nonfunctioning, the former being associated with clinical hyperparathyroidism. The majority of patients, nearly 91%, have nonfunctioning cysts.[4] In this group, women outnumber men 3 to 1, and the mean age of affected individuals is 43.3 years. In contrast, men are more likely to have functioning cysts, outnumbering women 1.33 to 1, and tend to be older with a mean age of 51.9 years.[2] The location of the cysts differs between the two groups. Nonfunctioning cysts are typically found in the inferior parathyroids and occur 60% of the time on the left side.[5] Functioning cysts are much less predictable and have been located anywhere from the angle of the mandible to the mediastinum.

The etiology of parathyroid cysts is uncertain, but four major theories suggest that they develop from embryological remnants of the third or fourth branchial pouch,[6] coalescence of microcysts,[7] simple retention of parathyroid secretions,[8] or cystic degeneration in preexisting adenomas.[9] No one theory completely explains their origin, and many factors probably contribute to their etiology.

There are histological differences between functioning and nonfunctioning cysts. Nonfunctioning cysts are simple cysts lined by a flattened-cuboid to low-columnar epithelium.[2,5] Several types of parathyroid cells are found in their walls—chief cells,[10] water-clear cells, and oxyphil cells[5]—but all three are not necessarily present. The presence of smooth muscle in the wall of some parathyroid cysts suggests that these may arise from branchial pouch remnants.[11]

Some functioning cysts lack an identifiable lining and are more properly termed pseudo-cysts.[2] They may contain foci of hemorrhage or necrosis and brown, turbid or even bloody fluid with hemosiderin-laden macrophages.[12] It is believed that these may arise from degenerating adenomas. Other functioning cysts are multilocular, complex lesions with thin walls and are found in close association with either an adenoma or hyperplastic gland.[2]

The pathogenesis of hypercalcemia in patients with functioning cysts has not been fully elucidated. Nests of parathyroid cells within the cysts may secrete PTH directly into the circulation; alternatively, PTH from the cyst's lumen may leak into the bloodstream.[11] In one instance, FNA of a parathyroid cyst was temporally related to the development of hypercalcemic crisis.[12] It was postulated that needle tracks opened holes in the cystic wall, which allowed fluid rich in PTH to leak into the circulation. This was the likely cause of worsening hypercalcemia in our patient following FNA.

The correct diagnosis of a parathyroid cyst requires three steps: consideration of parathyroid cysts in the differential diagnosis of a cystic mass in the neck, thyroid or elsewhere in the mediastinum; fine needle aspiration; and analysis of cyst fluid for PTH. Although rare, parathyroid cysts are being detected more frequently due to widespread application of FNA, and it is particularly important to distinguish parathyroid from thyroid cysts. The former typically produce a clear, colorless fluid, whereas the latter contain fluid that is amber or brown. The presence of amber, brown, or even hemorrhagic fluid, however, does not exclude the diagnosis of parathyroid cyst.

To further differentiate between the two, aspirated fluid should be analyzed for PTH. Although intact hPTH assays are gaining wider use, Birnbaum and Van Herle[13] suggest that the measurement of PTH using a mid-molecule assay may be the more appropriate test. They

report a case of a woman with a parathyroid cyst whose intact hPTH level was deceptively low, although her mid-molecule hPTH was elevated. They observed that parathyroid cysts occasionally produce fragments, rather than intact PTH, and that exclusive reliance on intact hPTH assay could lead to a missed diagnosis.

Once the diagnosis has been made, management depends upon whether the cyst is functioning or nonfunctioning. The definitive treatment for both remains surgical removal. This can be avoided, however, in nonfunctioning cysts by performing FNA. Complete disappearance of nonfunctioning cysts after FNA is well documented in the literature.[14] In one instance of a recurring nonfunctioning cyst, successful sclerosis was performed with injection of tetracycline, and surgery was avoided.[15] Observation without intervention may be appropriate in small, nonsymptomatic cysts. With functioning cysts, the consensus is that surgical removal is warranted.[2,11,15] Although our review of the literature failed to find any reports of multiple functioning cysts, we recommend surgical exploration of all four parathyroid glands. Care should be taken to remove each encountered cyst or adenoma, leaving as many of the remaining parathyroids intact as is possible.

In conclusion, parathyroid cysts are rare, but the diagnosis should be entertained in a patient with a cystic neck mass, especially one occurring in the lower poles of the thyroid or discovered in a patient with hypercalcemia. Diagnosis is best made by sending cyst fluid for PTH analysis using the mid-molecule hPTH assay, if available, or, if not, by measuring intact hPTH. Aspiration of functional cysts may worsen preexisting hypercalcemia, as in the patient we report, and may even lead to hypercalcemic crisis. Serum calcium levels should be monitored after aspiration of suspected, functioning parathyroid cysts. Nonfunctioning cysts may be cured by FNA with or without the use of a sclerosing agent, but functioning parathyroid cysts should be surgically removed.

REFERENCES

1. Goris D. Extirpation de trois lobules parathyroidiens kystiques. J Chir Ann Pathol Soc Belge 1905; 5:394–400

2. Rosenberg J, Orlando R, Ludwig M, Pyrtak LJ. Parathyroid cysts. Am J Surg 1982; 143:473–480

3. Crile G Jr, Perryman RG. Parathyroid cysts: report of five cases. Surgery 1953; 34:151–154

4. Layfield LJ. Fine needle aspiration cytology of cystic parathyroid lesions: a cytomorphic overlap with cystic lesions of the thyroid. Acta Cytologica 1991; 35:447–450

5. Waldron CA. Face, lips, tongue, teeth, oral soft tissues, jaws, salivary glands and neck. In Kissane JM (Ed): Anderson's Pathology, St. Louis, Mo, CV Mosby, 1990, pp 1095–1151

6. Troster M, Chiu HF, McLarty TD. Parathyroid cysts: report of a case with ultrastructural observations. Surgery 1978; 83:238–242

7. Castleman B, Mallory TB. The pathology of the parathyroid gland in hyperparathyroidism. Am J Pathol 1935; 11:1–80

8. Selye H, Ortega MR, Tuchweber B. Experimental production of parathyroid cysts. Am J Pathol 1964; 45:251–259

9. Rogers LA, Fitter B, Pette WBJ. Parathyroid cyst and cystic degeneration of parathyroid adenoma. Arch Pathol 1969; 88:476–479

10. Miyauchi A, Kakudo K, Fujimoto T, Onishi T, Takai S-I. Parathyroid cyst: analysis of the cyst fluid and ultrastructural observations. Arch Pathol Lab Med 1981; 105:497–499

11. Spitz AF. Management of a functioning mediastinal parathyroid cyst. J Clin Endocrinol Metab 1995; 80:2866–2868

12. Kobayashi A, Kuma K, Matsuzuka F. Exacerbation of hypercalcemia after needle biopsy of a parathyroid cyst. Ann Int Med 1989; 110:326–327

13. Birnbaum J, Van Herle AJ. Immunoheterogeneity of parathyroid hormone in parathyroid cysts: Diagnostic implications. J Endocrinol Invest 1989; 12:831–836

14. Ginsberg J, Young JEM, Walfish PG. Parathyroid cysts. JAMA 1978; 240:1506–1507

15. Sanchez A, Caretto H. Treatment of a nonfunctioning parathyroid cyst with tetracycline injection. Head Neck 1993; 15:263–265

Lessons From the Practice

Phillip

GARY S. REITER, MD, FACP, *Holyoke, Massachusetts*

Phillip Kennedy woke up later than usual on Monday, January 27, 1997. He had a headache and fever, and he planned to stay home from work. I awoke at 5:45 AM, tired after a weekend on call. As I dressed in the dark winter dawn, I looked forward to coming home early. But, Phillip Kennedy was to die that day, and I was destined to share in his death.

Phillip was 54 years old with diet-controlled diabetes and alcoholism in recovery. I had cared for him in my internal medicine practice for seven years. Phillip usually saw me three times a year for routine visits and his annual physical. He was a gregarious, affable man with red hair and a ruddy complexion. Our interactions were friendly, natural, affectionate, and at times, playful.

Phillip came to see me for his annual physical on Wednesday, January 22. He felt good and had no specific complaints. Phillip told me that, over Christmas, he had married June, the woman he had been living with for the past 12 years. June was 20 years his junior. Phillip said that there were parties surrounding the wedding and that he had started to drink again. He said that he was just celebrating with friends, not drinking excessively. Everything was under control.

Phillip's exam was normal except that his liver was firm and moderately enlarged. I told Phillip to stop drinking and ordered a complete blood cell count and a chemistry panel including liver studies. I called Phillip the next day to remind him to abstain from alcohol and to tell him that his lab tests were normal.

I was on call the following weekend—the nights were particularly brutal, with multiple phone calls and time spent in the intensive care unit until the early morning hours. I rearranged my schedule on Monday the 27th so that I could be done by 3:45 that afternoon and possibly stop by the gym or take a late afternoon nap; probably the latter.

June called Monday morning to ask for an urgent appointment. She said that Phillip had been sick all weekend and needed to be seen. Phillip was double-booked into the 1:00 PM slot. After returning from lunch, I brought Phillip and June back into the exam room. I hadn't met June before. Phillip and I joked briefly about his new, young bride as he introduced us. After he got undressed, Phillip said that he felt "generally lousy" with a headache, a fever, and no other specific symptoms. Although Phillip and June both initially reported that he hadn't had any alcohol for the past two days, June later acknowledged that Phillip had been drinking much more heavily than he had previously owned up to.

On exam, Phillip had a temperature of 103° F, the same hepatomegaly noted five days previously, and a faint, yellow tint to his ruddy complexion. No other part of the exam was remarkable. He had no tremor or confusion and was definitely not experiencing alcohol withdrawal. I sent Phillip downstairs to the hospital for a chest x-ray and some blood work, feeling that he probably had a viral syndrome, an occult pneumonia, or possibly alcoholic hepatitis. His recent normal lab test results and relatively normal exam reassured me that his condition was probably a benign process.

Thirty minutes later, the lab called me with several panic values. Phillip's platelet count was 30 thousand/cc, white blood cell count was 19 thousand/cc, bilirubin was 13 mg/dl, and his serum glutamic-oxalocetic transeminase was 560 U/liter. While I rechecked Phillip's lab data from the previous week, I asked the lab tech to make sure that the results she had given me were for Phillip. She confirmed that the results were Phillip's from today even though the same lab tests had been normal five days earlier! I asked the lab tech to send him back to my office immediately.

When Phillip and June returned, he was acting confused. He had lost control of his bowels while waiting in the lab. I told them that he needed to be admitted to the hospital. Phillip insisted on cleaning himself up in the office rest room before going to the hospital admissions office. He seemed to take an awfully long time in the bathroom. Occasionally, I would peek in and tell him to hurry. After several minutes, I checked on him once more and told June that I was going to see a couple of other patients. I asked her to get me when Phillip was done so that we could get him down to admissions.

While I was with the next patient, June knocked on the door. Crying, she said she needed my help. The strong odor of feces was present as I approached the partially open rest room door. Phillip was now completely

(Reiter GS. Phillip. West J Med 1999; 170:121–123)

From the University of Massachusetts, Holyoke, Massachusetts.
Reprint requests to Gary Reiter, MD, University of Massachusetts, 15 Hospital Drive, Suite 403, Holyoke, MA 01040 (e-mail: lazzreit@javanet.com).

naked; mottled and markedly jaundiced; unconscious and smeared with feces; still on the toilet but slumped against the wall. The stench was overwhelming.

Phillip had no pulse as I slid him off the toilet. I began CPR by myself while my office staff called a "Code Blue." Phillip recovered spontaneous respiration and pulse as the code team arrived. Before accompanying Phillip down to the emergency room (ER), I tried to reassure June that he would be all right. Phillip looked somewhat better in the ER. He was talking and said he felt okay. Yet he appeared to be in septic shock with hypotension, warm mottled skin, and anuria. I re-examined Phillip; ordered pressors, fluids, and antibiotics; arranged for an intensive care unit ICU bed; and returned to my office.

By that time, it was 4:00 PM and the rest of the afternoon's patients were still waiting for me. Neither I nor my office staff had thought of rescheduling them. My next patient, Mrs Trumble, a lovely, 84-year-old woman with multiple medical problems, was one of my favorites. As I entered the exam room, she asked, "Are you all right, doctor?"

Christ! How could I answer such a question? How long could I keep up the conceit that everything goes along according to plan, and I'm captain of the ship? I told Mrs Trumble that I had been caring for someone who unpredictably had become quite ill, and that I was disturbed, distracted, and saddened by it. I excused myself to check the roster of patients for the rest of the day. I asked my office staff to reschedule all but the most urgent patients and then returned to finish my visit with Mrs Trumble.

I finished in the office around six that evening and went to the ICU. Although Phillip's blood pressure had stabilized and he was no longer mottled, Phillip was still anuric and only minimally responsive. Before going home for dinner, I reviewed Phillip's care with the nurses and spoke to June. I checked out with my colleague who was covering, but told the answering service to call me for matters related to Phillip Kennedy.

By the time I got home, our two older boys had had dinner, and our infant had gone to sleep. I shared a glass of wine with my wife, telling her about Phillip. About halfway through dinner, the answering service called with the ICU on the line. The nurse, Candy, said that they couldn't keep Phillip's pressure up despite maximum doses of dopamine. She also said that Phillip was starting to have runs of ventricular tachycardia as well as some profound bradycardia. I told Candy that I'd be right in and asked her to get June on the phone for me.

I told June that things didn't look good for Phillip. June gasped and started to cry. I told her that I was coming into the hospital and would be there in a few minutes. Just then I could hear, "Code Blue ICU" coming over the hospital loud speaker. June screamed, "Oh, shit! It's Phillip," and dropped the phone.

When I arrived at the ICU, the code team was still working on Phillip, but he was already dead. The head of the team looked at me, and I told him to stop. I walked back to a room behind the nurses station where June was sitting with a couple of nurses. I sat down next to June and took her hand. She sobbed, "I can go along with some tests, but I can't lose him. I can go along with a few days in the hospital, but I can't lose him." I sat quietly with June as she spoke. Finally, I said, "It's bad, it's very, very bad, June. And it's not fair—sometimes terrible things happen." June looked up at me, her eyes open and wild, "He's not dead, is he?" I looked at June, still holding her hand, "Yes, June, Phillip's dead."

"Ahhhhhhhhh no!" June wailed as she fell to the floor, rolling around, shrieking uncontrollably. After a few minutes, I tried to touch June, but she pulled away. "No! Don't touch me!" She sat on a chair and rocked back and forth. "I want to see Phillip." June's parent's arrived as I led her to Phillip's room.

June's parents and I sat down in the room as June climbed into bed with Phillip. She lay with him for a long time; at first quietly, then caressing him, kissing his hands and face, and then laying her head on his chest. I left the room and waited for June at the nurses' station.

When June came out, we hugged each other and wept. I told her that I would be available for her when she needed me. June agreed to my request for an autopsy. We both needed to know just what had set off this horrific storm of events. I left the ICU, overwhelmed with emotion, and stopped in the hospital chapel on the way to my car. Kneeling at the prie-dieu, I rested my head on my folded arms and cried for a long time. "God, why do you do these things?"

Phillip's autopsy showed that he had died of an hepatic abscess, possibly secondary to diverticular disease. The mortality for hepatic abscess, if antibiotics are started after the onset of sepsis, is reported as greater than 30%.

Death is no stranger to me. I have spent much of my career treating people with HIV, and I serve as a medical director for our local hospice. The thousands of deaths I've been involved with have given me the false sense that I somehow understand death; that death has a pace and a rhythm; that I don't always know when death will happen, but that I know it is happening when it is happening. I am familiar with the physical, emotional, psychological, and spiritual phases people go through as they die. Many of us in the hospice world refer to death as a birth-like event. We often refer to ourselves as "midwives to death." In this model, death is an unfolding. It's a process we can watch, anticipate, ride . . . surf.

Phillip's death was not an unfolding. It was not a birth. It was a miscarriage. There was no guidance in this event. June and I took a horribly unpredictable ride into hell. In the days that followed Phillip's death I began to ask myself, "Why did this have to happen in my office? Why did I have to be involved?" After all, if Phillip had stayed home two more hours before coming in, if his appointment had been at 3:00 PM instead of 1:00 PM, he would have died at home. It would have still been horrible for June, but I would have been spared. Why did I have to be part of Phillip Kennedy's death?

My deep spiritual belief is that things don't happen by accident. I had to partake in Phillip's death. I had to be present for June, during and after this horrific event, which has inextricably bound us together. Bad things happen in our lives that we cannot control. Phillip's death could not be prevented. My role was not to prevent Phillip's death, but to soften its blow for June and her family. June needed me to share Phillip's death as a witness, a mirror in which to search for meaning. My professional experience with death as well as some tragic deaths in my own life prepared me to participate in Phillip's death as a physician, a friend, and a fellow mortal. I thank God for the strength gained over the course of my life to help people in need. And, I pray that I won't be called upon again for a good, long time.

In Memoriam

Dr Robert N. Treadwell

Robert N. Treadwell, MD, of Fortuna, California, died on November 25, 1998, at the age of 86. A graduate of Stanford Medical School, Dr Treadwell served in the US Army as a member of the Stanford Unit/59th Evacuation Hospital Service in the European-African Mideastern Theater. Later, Dr Treadwell was in general practice in the Scotia-Rio Dell area until his retirement in 1987. He served as Chief of Staff at Redwood Memorial Hospital for one term, and he was a member of the Humboldt-Del Norte County Medical Society.

Poem

* * *

I dream that Death is a turtle

If you had flown in like a bat
and banged around,
all search and disappointment,
I might have fled the room,
afraid of your confusion.

But you moved in slowly,
unconcerned and steady,
so heavy with your age
that I walked out to meet you
impatient and unafraid.

Roxanne Lanier
Greenbrae, California

Classified Advertisements

The rate for each insertion is **$1.50 per word, with a 30 word ($45) minimum.** Confidential box number charge: $10 each month.
A word is defined as one or more letters bounded by spaces. The following gives some examples:

Linda H. Clever, MD	= 4 words	allergy/immunology	= 1 word
Send CV	= 2 words	Sacramento, CA 95817	= 3 words
A	= 1 word	804-979-8034	= 1 word
February 22, 1997	= 3 words		

Classified display rate $70 per inch. Maximum sizes: 1 column by 5" or 2 columns by 2" (2-1/8" per column). Larger classified ad space by special arrangements.
Copy for classified advertisements should be received not later than **first of the month preceding issue. All copy must be typed or printed.** Classified advertisers using Box Numbers forbid the disclosure of their identity; your inquiries in writing will be forwarded to Box Number advertisers. Although *The Western Journal of Medicine* believes the classified advertisements in these columns to be from reputable sources, we do not investigate the offers made and assume no liability concerning them. The right is reserved to reject, withdraw, or modify all classified advertising copy in conformity with the decisions of the Advertising Committee.

Please Type or Print Advertising Copy

Classified Advertisements Are Payable in Advance
CLASSIFIED ADVERTISEMENTS, THE WESTERN JOURNAL OF MEDICINE
P.O. BOX 7690, SAN FRANCISCO, CA 94120-7690
(415) 882-5177; FAX (415) 882-3379
Ads may be placed online at www.wjmed.com

PHYSICIANS WANTED

PHYSICIAN Outpatient Clinic. The County of San Mateo has an immediate opening for a Board certified/eligible physician for our new South San Francisco clinic opening in April 1999. Two years experience providing primary care services to a predominantly adult population. Spanish speaking preferred. Full-time position with excellent benefits and competitive salary. Fax CV to (650) 573-2458, or mail to 455 County Center, Redwood City, CA 94063. EOE. COUNTY OF SAN MATEO

ASSISTANT or ASSOCIATE PROFESSOR, DIVISION OF NEPHROLOGY. The University of California, Davis, School of Medicine, Department of Internal Medicine is recruiting a full-time Assistant or Associate Professor. The position requires demonstrated leadership abilities in the subspecialty, strong clinical skills, excellence in teaching. Candidates must be Board certified in Internal Medicine and Board eligible or Board certified in the subspecialty of Nephrology. Please forward Curriculum to: George Kaysen, M.D., Ph.D., c/o Julie Mustard, Department of Internal Medicine, University of California, Davis, 4150 V Street, 3100 PSSB, Sacramento, CA 95817. This position is open until filled but no later than February 28, 1999. The University of California is an affirmative action/equal opportunity employer.

California Department of Corrections

Health Care Services Division

HEALTH CARE MANAGER
CHIEF MEDICAL OFFICER

The California Department of Corrections has practice opportunities for BC/BE CA Licensed Physicians at various correctional facilities. You will be responsible for the management and quality assurance of the Medical Program; Pharmacy; Medical Records; Mental Health and Dentistry. Must be licensed to practice in California. Current opportunities exist at:

- California State Prison, Sacramento
- California State Prison, Corcoran
- High Desert State Prison, Susanville
- California State Prison, Corcoran
- Wasco State Prison Receptian Center, Wasco

You will enjoy outstanding State of California Civil Service Benefits, with 13 paid holidays, health/dental/vision plans, generous vacation plan, professional liability coverage, safety retirement and much more.

To apply, contact Medical Recruiter, Health Care Services Division, P.O.Box 942883, Sacramento, CA 94283-0001. Phone: (916) 327-7081 or toll free (888) 232-4584, Fax: (916) 327-1436. Online: www.spb.ca.gov. EOE

HEALTH CARE SERVICES DIVISION
CALIFORNIA DEPARTMENT OF CORRECTIONS
PUBLIC SAFETY. PUBLIC SERVICE

2/99

Defining the future of healthcare

Take a closer look at the future of healthcare, a future taking shape at The Cleveland Clinic Foundation. We have built the region's largest and most prestigious healthcare organization through a commitment to international leadership and top quality patient care, education and research.

The recent partnership between The Cleveland Clinic and the Wooster Clinic has created excellent opportunities for Board Certified/Eligible:

Internists • Cardiologists
Pulmonologists • Gastroenterologists

Enjoy the advantages of practicing personalized, community-based medicine combined with access to state-of-the-art facilities at The Cleveland Clinic's main campus. The Wooster, Ohio location offers a wonderful, family-oriented community, in a progressive college town. Become part of an expanding, multispecialty medical group.

Qualified professionals will receive a competitive salary, excellent benefits and paid meeting and vacation time. Send curriculum vitae to: **Attn: John Ferkan, Manager, Physician Recruitment, The Cleveland Clinic Foundation, P.O. Box #606140, Cleveland, OH 44106. Fax: 216-738-4059. email: ferkonj@cesmtp.ccf.org.** We are proud to be an equal opportunity employer. Smoke/drug-free environment.

Visit our homepage on the world wide web: **www.ccf.org**.

THE CLEVELAND CLINIC
Every Life Deserves World Class Care

PHYSICIANS WANTED

Physician needed part-time (.2–.5 FTE) to provide geriatric primary care and some adult internal medicine for our *Over 60 Health Center* in East Oakland. Board Certification IM or FP required. Community clinic/minority background experience highly desirable. Contact: Dr. Floyd Huen, Medical Director (510) 597-8010 Ext. 407. Resume: LifeLong Medical Care, 1860 Alcatraz Avenue, Berkeley, CA 94703.

YELLOWSTONE NATIONAL PARK. Physician to cover outpatient clinic, emergency room, and inpatient at Lake Hospital from May to September 1999. Send CV to: Yellowstone Park Medical Services, 707 Sheridan Avenue, Cody, WY 82414 or call 1-800-654-9447 (ext. 462).

PSYCHIATRIST

Full time position in central California; convenient to San Francisco, Lake Tahoe & West coast. Working with large community mental health program with UC Davis link; Adult Outpatient; no call; advanced multi-disciplinary team. Please call Kathy Lopez, Human Resources; or Randall Stenson, M.D.; or Roger Speed, Director, at:
(209) 468-8750

IDAHO

Make One Of America's Best Places to Live Even Better.

Where You'll Work.
Primary Health, Idaho's largest, fastest-growing integrated health care system whose network of family medicine immediate care centers, by-appointment family practitioners, pediatricians and OB/GYNs serves beautiful southern Idaho.

Where You'll Live.
In a great place to raise a family with quality schools, incredible outdoor recreation and a rural atmosphere close to a metropolitan area with a beautiful performing arts center, excellent hospitals and professional sports.

What You'll Get.
The financial backing and medical resources of a major health care network. A competitive salary, ownership options, flexible work and call schedules, professional growth, full benefits including medical and dental and much more

Submit CV and questions to:
BECKY NELSON
(800) 688-5008 ext. 507 • FAX (208) 344-4262
Physician Recruitment
800 Park Boulevard, Suite 760
Boise, Idaho 83712

Primary Health

Advertising Index

eBMJ . . . . . 2nd Cover
BMJ Reprints . . . . . 3rd Cover
BMJ Bookshop . . . . . 4th Cover
J Med Ethics . . . . . Page 128

Reprints

Any article printed in *WJM* can be purchased in quantities of 100 or more. Printed on fine quality journal stock. Prices are based upon article length and quantity ordered.

Contact Marsha Fogler, Medical Reprint Services, PO Box 3227, Cherry Hill, NJ 08034
Phone (800) 482-1450;
Fax (609) 482-7414;
E-Mail: fogler@erols.com

The California Academy of Family Physicians invites you to attend our
51st Annual Scientific Assembly
February 12-14, 1999 in Beautiful San Diego

Featuring:

- A keynote address by Nancy Dickey, MD, President of the American Medical Association & Family Physician
- 9 clinical lectures on a wide array of topics
- 4 procedural workshops
- 5 practice management/clinical seminars
- An unforgettable drama about teen health concerns
- Panel discussion on implications of genetic testing
- 6 interactive, open discussion forums
- Preconference Internet and Smart Coding seminars
- 9 satellite CME Sessions at no additional cost

Keynote Speaker: Nancy Dickey, MD

Receive up to 43.5 hours of CME Credit

Outstanding Workshops & Seminars

CALIFORNIA ACADEMY OF FAMILY PHYSICIANS

For details and registration info, call 415-394-9121
Or — register online at www.FamilyDocs.org/Register

PUBLISHED BIMONTHLY

BMJ Publishing Group

JOURNAL OF

Medical ETHICS

Journal of the Institute of Medical Ethics

Editor: Raanan Gillon

First published in 1975, *Journal of Medical Ethics* is a leading international journal featuring interdisciplinary articles on ethical aspects of health care. With an increase in frequency from quarterly to bimonthly, the journal offers original articles, case conferences, editorials, book reviews, correspondence, news and notes.

A Selection of Recent Papers:

"Goodbye Dolly?" The ethics of human cloning
John Harris

At the coalface - medical ethics in practice: First, do no harm
Scott Groudine and Philip D Lumb

Patients' rights in England and the United States of America: The Patients's Charter and the New Jersey Patient Bill of Rights: a comparison
Melanie H Wilson Silver

Subscription Rates

Institutional: Worldwide £132, USA Only $214

Personal: Worldwide £90, USA Only $146

Student Rate: Worldwide £47, USA Only $76*

* (Please send proof of student status)

VISIT OUR HOMEPAGE ON: www.jmedethics.com

ORDER FORM

Journal of Medical Ethics

ISSN 0306 6800 Publication: Bimonthly

1999 Subscription Rate: Institutional: Worldwide £132, USA Only $214
Personal Rate: Worldwide £90, USA Only $146
Student Rate: Worldwide £47, USA Only $76*
***(Please send proof of student status)**

☐ Send me instructions to Authors

☐ Send me a free sample copy

☐ Enter my subscription, starting from: .....

☐ I enclose a cheque for £/$ .....
(Payable to BMJ)

☐ Charge my credit card £/$.....

☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐

American Express/Visa/Mastercard/Delta/Switch
(delete as appropriate)

Switch Issue Number .....

Expiry date .....Signature .....
(Your signature is essential when paying by credit card)
If your billing address differs from below, please advise us

Name.....

Address.....

.....

Postcode .....Country .....

N.B. Subscribers in the following countries must add tax to the quoted sterling price unless they can provide a registration number: Canada - 7% GST, Italy and Spain - 4% IVA, Ireland - 21%, Germany - 7% MWS, Belgium - 6% TVA/BTW and France - 20.6% TVA

Send orders to: **BMJ Publishing Group, Journals Marketing Dept., PO Box 299, London WC1H 9TD, UK.**

Orders in the U.S: **BMJ Publishing Group, Box 509A, Kennebunkport, ME 04046, USA.**
Tel: 1-800-2-FON-BMJ Fax: 1-800-2-FAX-BMJ

For reprints opportunities, please contact:

Sheila Williams (Quotations)
Tel: +44 (0)171 383 6305 Fax: +44 (0)171 383 6699
Email: swilliams@bmjgroup.com

Sheila Rowe (Sales Enquiries)
Tel: +44 (0)171 383 6450 Fax: +44 (0)171 383 6556
Email: jwheeler@bmjgroup.com

For enquiries within USA & Canada, please contact: Marsha Fogler
Tel: 1(800) 482 1450 or 1(609) 482 9665 Fax: 1(609) 482 7414
Email: fogler@erols.com

BMJ Bookshop

TITLES Extensive database of medical and related titles

INFORMATION Book information includes contents lists and descriptions

SEARCH User friendly searching by key word and subject category

ORDERING Flexible and secure online ordering options

BESTSELLERS Top 10 and new title features

bmjbookshop

The online bookshop for medical professionals – open 24 hours a day

OFFICIAL JOURNAL OF

KA ICAL ION | ARIZONA MEDICAL ASSOCIATION | CALIFORNIA MEDICAL ASSOCIATION | DENVER MEDICAL SOCIETY | IDAHO MEDICAL ASSOCIATION | NEVADA STATE MEDICAL ASSOCIATION | NEW MEXICO MEDICAL SOCIETY | UTAH MEDICAL ASSOCIATION | WASHINGTON STATE MEDICAL ASSOCIATION | WYOMING MEDICAL SOCIETY

DISPLAY SHELVES

The Western Journal of Medicine

VOLUME 170 • NUMBER 3 MARCH 1999

ARTICLES

137 Effect of Incentives on the Use of Indicated Services in Managed Care
SZ PANTILAT, M CHESNEY, AND B LO

143 Cluster of Postinjection Abscesses Related to Corticosteroid Injections and Use of Benzalkonium Chloride
RK OLSON, RE VOORHEES, HE EITZEN, H ROLKA, AND CM SEWELL

148 Cancer Screening Practices Among Primary Care Physicians Serving Chinese Americans in San Francisco
MM LEE, F LEE, S STEWART, AND S MCPHEE

156 Prevalence and Correlates of Hepatitis C Virus Infection Among Inmates Entering the California Correctional System
JD RUIZ, F MOLITOR, RK SUN, J MIKANDA, M FACER, JM COLFORD JR, GW RUTHERFORD, AND MS ASCHER

161 Primary Mediastinal Malignancies: Findings in 219 Patients
R TEMES, T CHAVEZ, D MAPEL, L KETAI, R CROWELL, C KEY, F FOLLIS, S PETT, AND J WERNLY

167 Physical Fitness, Aging, and Sexuality
WM BORTZ II AND DH WALLACE

ALERTS, NOTICES, AND CASE REPORTS

170 Alternating Transient Dense Hemiplegia Due to Episodes of Hypoglycemia
MA WATTOO AND HH LIU

172 Pathologic Fracture Occurring 22 Years After Diagnosis of Hairy Cell Leukemia: Case Report and Literature Review
KS SNELL, MM O'BRIEN, K SENDELBACH, AND R MARTINO

174 Endotracheal Intubation and Mechanical Ventilation Following Respiratory Arrest From High Altitude Pulmonary Edema
JA LITCH

EDITORIAL

177 Identifying Infectious Diseases in Prisons: Surveillance, Protection, and Intervention
MC WHITE

CORRESPONDENCE

178 Cigarette Smoking Prevention—Physicians Should Teach by Example
TO CHENG

178 Drs Pérez-Stable and Fuentes-Afflick Respond
EJ PÉREZ-STABLE AND E FUENTES-AFFLICK

OTHER FEATURES

132 Continuing Medical Education Activities
179 Poetry
182 Classified Advertising
185 Instructions for Authors

Detailed Table of Contents: 130, 131

Affiliated Clinical Investigation Societies: the Western Association of Physicians; the Western Society for Clinical Investigation; the Western Section, American Federation for Medical Research; the Western Society for Pediatric Research; the Western Region, Society for Investigative Dermatology

THE FRANCIS A. COUNTWAY
LIBRARY OF MEDICINE
BOSTON, MA

APR 12 1999

Full text, free access.

– Fully searchable archive –

– 150 topic collections –

– Customised email alerting –

– Rapid responses –

– Enhanced articles –

– Extra news stories –

– Direct Medline access –

– Jobs, courses, and careers –

And we don't ask you to pay, subscribe, register, provide passwords, or fill in interminable online questionnaires.

www.bmj.com

THE FRANCIS A. COUNTWAY
LIBRARY OF MEDICINE
BOSTON, MA

The Western Journal of Medicine®

SINCE 1902

P.O. BOX 7690 • SAN FRANCISCO, CALIFORNIA 94120-7690
221 MAIN STREET • SAN FRANCISCO, CALIFORNIA 94105
TELEPHONE (415) 974-5977; FACSIMILE (415) 882-3379; E.MAIL wjmsf@pacbell.net

APR 12 1999

MICHAEL S. WILKES, *Editor*
MIRIAM SHUCHMAN, *Editor*

CATHERINE NANCARROW, *Editorial Manager*
NEIL POPPMACHER, *Production Manager*
RUTH STAUNTON, *Business Manager*

editorial communications to CATHERINE NANCARROW • business communications to RUTH STAUNTON

Official Journal of the Alaska State Medical Association, the Arizona Medical Association, the California Medical Association, the Denver Medical Society, the Idaho Medical Association, the Nevada State Medical Association, the New Mexico Medical Society, the Utah Medical Association, the Washington State Medical Association, and the Wyoming Medical Society.

Affiliated Clinical Investigation Societies: the Western Association of Physicians; the Western Society for Clinical Investigation; the Western Section, American Federation for Medical Research; the Western Society for Pediatric Research; the Western Region, Society for Investigative Dermatology.

SPECIAL EDITORS

Special Editor for Arizona
Marshall B. Block, Phoenix, AZ

Special Editor for Denver
David Shander, Denver, CO

Special Editor for Idaho
E. R. W. Fox, Coeur d'Alene, ID

Special Editor for Nevada
Anton P. Sohn, Reno, NV

Special Editor for New Mexico
I. Brian Taylor, Carlsbad, NM

Special Editor for Utah
C. Basil Williams, Salt Lake City, UT

Special Editor for Washington
David Hopkins, Federal Way, WA

Special Editor for Wyoming
Joseph P. Murphy, Casper, WY

ASSISTANT EDITORS

Clinical Investigation
H. Benfer Kaltreider

Health and Public Policy
Ralph Crawshaw

International Health
Anvar Velji

Lessons From the Practice
Stephen J. McPhee
Jonathan E. Rodnick

Medical Staff Conferences
Nathan M. Bass

Poetry
Margaret Kaufman

Primary Care Medicine
Stephen J. McPhee
Terrie Mendelson

Radiologic Cases
Jonathan M. Levy

EDITORIAL BOARD

Editor Emeritus
Malcolm S. M. Watts, San Francisco, CA

Anesthesiology
Carol Lake, Sacramento, CA

Biostatistics and Epidemiology
Virginia L. Ernster, San Francisco, CA

Cardiac and Thoracic Surgery
Norman E. Shumway, Stanford, CA

Dermatology
Clifton R. White Jr, Portland, OR

Emergency Medicine
William A. Boehm, Alamogordo, NM

General and Family Practice
Norman Kahn, Kansas City, MO
Thomas E. Norris, Seattle, WA
Joe Schoeber, Casper, WY

Internal Medicine
Albert Deisseroth, Houston, TX
Alan Fogleman, Los Angeles, CA
Patricia Gabow, Denver, CO
John H. Holbrook, Salt Lake City, UT
Philip Hopewell, San Francisco, CA
Irwin J. Schatz, Honolulu, HI
Walter E. Stamm, Seattle, WA
Reginald Strickland, Albuquerque, NM
Stephen I. Wasserman, San Diego, CA

Neurology
Robert Collins, Los Angeles, CA
John Greenlee, Salt Lake City, UT
Leslie Wiener, Los Angeles, CA
Earl Zimmerman, Portland, OR

Neurosurgery
George A. Ojemann, Seattle, WA
Robert F. Spetzler, Phoenix, AZ

Nuclear Medicine
Jerold M. Lowenstein, San Francisco, CA

Obstetrics and Gynecology
Daniel Mishell Jr, Los Angeles, CA

Occupational Medicine
Linda Rosenstock, Washington, DC

Ophthalmology
Sandy Feldman, La Jolla, CA

Orthopedics
Thomas DeCoster, Albuquerque, NM

Pathology
Ronald Weinstein, Tuczon, AZ

Pediatrics
Allen W. Mathies Jr, Pasadena, CA
Diane Wara, San Francisco, CA

Pharmacology
Rubin Bressler, Tucson, AZ

Physical Medicine and Rehabilitation
Julie G. Madorsky, Pomona, CA

Preventive Medicine and Public Health
Joseph L. Lyon, Salt Lake City, UT

Psychiatry
J. Christian Gillin, San Diego, CA
Lewis Judd, La Jolla, CA

Radiology
Gary Glazer, Stanford, CA
Michael L. Manco-Johnson, Denver, CO
Albert A. Moss, Seattle, WA

Surgery
Haile T. Debas, San Francisco, CA
Alex G. Little, Las Vegas, NV

Urology
Linda Shortliffe, Stanford, CA

Senior Members at Large
Thomas Elmendorf, Davis, CA
Edgar Wayburn, San Francisco, CA

ADVISORY BOARD, CLINICAL INVESTIGATION

Brian A. Cason, San Francisco, CA
John Christenson, Salt Lake City, UT
Kari Connolly, San Francisco, CA
Bruce W. Goldberg, Portland, OR
Philip Goodman, Reno, NV
Roy Jones, Albuquerque, NM
Howard Lien, Tucson, AZ
Barbara M. Lippe, Los Angeles, CA
Michael W. McDermott, San Francisco, CA
Jeanette Mladenovic, Denver, CO
Kenneth M. Moser, San Diego, CA
James C. Orcutt, Seattle, WA
John Owings, Sacramento, CA
Robert Robbins, Stanford, CA
Henry Rosen, Seattle, WA
Mary H. Samuels, Portland, OR
George A. Sarosi, San Jose, CA
Jeffrey Saver, Los Angeles, CA
David Schriger, Los Angeles, CA
Jack H. Simon, Denver, CO
Peggy Sue Weintrub, San Francisco, CA
Owen M. Wolkowitz, San Francisco, CA

DISPLAY ADVERTISING INFORMATION

CONTACT: Alan Walker, BMJ Publishing Group, BMA House, Tavistock Square, London WC1H 9JR, UK • (+44) 171-383-6226/FAX (+44) 171-3B3-6556. Email: awalker@bmj.com

Advertisements—The journal is published the second week of the month. Display advertising must be received no later than the first of the month preceding issue. Advertising rates will be sent on request. Acceptance of advertising is contingent upon approval by the Publisher.

The journal reserves the right to reject any advertisement.

CLASSIFIED ADVERTISING

CONTACT: Ruth Staunton, The Western Journal of Medicine, P.O. Box 7690, San Francisco, CA 94120-7690 • (415) BB2-5177/FAX (415) B82-3379.

SUBSCRIPTION INFORMATION

The subscription price is $70 per year and $130 for 2 years in the United States and Canada (US funds); $B5/$160 in all other countries. Institutional rate in the United States is $120/$240; $130/$260 all other countries. Single copies are $15. Address all subscription communications to:

BMJ Publishing Group, P.O. Box 590A, Kennebunkport, ME 04046 • B00-2-FON-BMJ • 800-2-FAX-BMJ. E-mail: bjpaige@cybertours.com

Allow six weeks for subscriptions to begin. Past issues must be bought individually. So long as reserve stocks are available, missing issue requests from subscribers are honored for up to six months after the issue date. Thereafter, the single copy rate of $15 is applicable for each issue available.

Change of Address—Requests for change of address should give both the old and new address. Allow six weeks for changeover.

SUBMITTING MANUSCRIPTS

Manuscripts for consideration should be sent to the editorial manager, C. Nancarrow, The Western Journal of Medicine, P.O. Box 7690, San Francisco, CA 94120-7690.

"Instructions for Authors"—A complete guide to manuscript submission and *WJM* style available from the publisher. Manuscripts may be prepared in accordance with the "Uniform Requirements for Manuscripts Submitted to Biomedical Journals."

PUBLISHER

Copyright © 1999 by the British Medical Journal Publishing Group • Owned and Published by BMJ Publishing Group and UCSF Stanford Healthcare

All material subject to this copyright appearing in THE WESTERN JOURNAL OF MEDICINE may be photocopied for the noncommercial purpose of scientific or educational advancement. Volumes begin with January and July.

THE WESTERN JOURNAL OF MEDICINE (ISSN 0093-0415/USPS 084 480) is published monthly by BMJ Publishing Inc, 221 Main St., San Francisco, CA 94105. (Mail correspondence to WJM–BMJ Publishing Inc., P.O. Box 7690, San Francisco, CA 94120-7690. Periodicals postage paid at Easton, Pennsylvania.

POSTMASTER: Send address changes to *The Western Journal of Medicine*, P.O. Box 7690, San Francisco, CA 94120-7690.

The Western Journal of Medicine

VOLUME 170 • NUMBER 3 • MARCH 1999

CONTENTS

ARTICLES

137 **Effect of Incentives on the Use of Indicated Services in Managed Care**

STEVEN Z. PANTILAT, MD; MARGARET CHESNEY, PhD; and BERNARD LO, MD

From the Division of General Internal Medicine, Department of Medicine, University of California, San Francisco, California; the Program in Medical Ethics, University of California, San Francisco, California; and the Center for AIDS Prevention Studies, University of California, San Francisco, California.

143 **Cluster of Postinjection Abscesses Related to Corticosteroid Injections and Use of Benzalkonium Chloride**

REBECCA K. OLSON, PhD; RONALD E. VOORHEES, MD, MPH; HAROLD E. EITZEN, PhD; HENRY ROLKA, MS; and C. MACK SEWELL, DrPH, MS

From the Epidemic Intelligence Service and the Division of Prevention Research and Analytic Methods, Epidemiology Program Office, Centers for Disease Control and Prevention, Atlanta, Georgia; Office of Epidemiology, New Mexico Department of Health, Santa Fe, New Mexico.

148 **Cancer Screening Practices Among Primary Care Physicians Serving Chinese Americans in San Francisco**

MARION M. LEE, PhD; FLORENCE LEE, MPH; SUSAN STEWART, PhD; and STEPHEN MCPHEE, MD

From the Department of Epidemiology and Biostatistics, University of California, San Francisco, California; Northern California Cancer Center, Union City, California; and Department of Medicine, University of California, San Francisco, California.

156 **Prevalence and Correlates of Hepatitis C Virus Infection Among Inmates Entering the California Correctional System**

JUAN D. RUIZ, MD, DrPH; FRED MOLITOR, PhD; RICHARD K. SUN, MD, MPH; JOHN MIKANDA, MD, MPH; MATTHEW FACER, MS; JOHN M. COLFORD JR., MD, PhD; GEORGE W. RUTHERFORD, MD; and MICHAEL S. ASCHER, MD

From the California Department of Health Services, Sacramento, California, Office of AIDS, HIV/AIDS Epidemiology Branch, the Maternal and Child Health Branch, and the Viral and Rickettsial Disease Laboratory; the University of California at Berkeley, Berkeley, California; and the University of California at San Francisco, San Francisco, California.

161 **Primary Mediastinal Malignancies: Findings in 219 Patients**

ROY TEMES, MD; THERESA CHAVEZ, CTR; DOUGLAS MAPEL, MD; LOREN KETAI, MD; RICHARD CROWELL, MD; CHARLES KEY, MD; FABRIZIO FOLLIS, MD; STUART PETT, MD; and JORGE WERNLY, MD

From the Department of Surgery, Division of Thoracic and Cardiovascular Surgery; the New Mexico Tumor Registry; the Department of Medicine; and the Department of Radiology, University of New Mexico School of Medicine, Albuquerque, New Mexico.

167 **Physical Fitness, Aging, and Sexuality**

WALTER M. BORTZ, II, MD and DOUGLAS H. WALLACE, PhD

From the Palo Alto Medical Foundation, Stanford University School of Medicine, Palo Alto, California; and the Department of Psychiatry, University of California, San Francisco, California.

ALERTS, NOTICES, AND CASE REPORTS

170 **Alternating Transient Dense Hemiplegia Due to Episodes of Hypoglycemia**

MUHAMMAD A. WATTOO, MD and HANS H. LIU, MD, FACP

From the Department of Medicine, University of Pennsylvania Health System/Presbyterian Medical Center, Philadelphia, Pennsylvania; and Allegheny University Medical Practices, Allegheny Health, Education and Research Foundation, Philadelphia, Pennsylvania.

172 **Pathologic Fracture Occurring 22 Years After Diagnosis of Hairy Cell Leukemia: Case Report and Literature Review**

KENNETH S. SNELL, MD; M. MARGARET O'BRIEN, MD; KARLA SENDELBACH, MD; and ROY MARTINO, MD

From the Departments of Pathology and Internal Medicine, University of South Alabama, Mobile, Alabama.

174 **Endotracheal Intubation and Mechanical Ventilation Following Respiratory Arrest From High Altitude Pulmonary Edema**

JAMES A. LITCH, MD, DTMH

From the Himalayan Rescue Association, Kathmandu, Nepal.

EDITORIAL

177 **Identifying Infectious Diseases in Prisons: Surveillance, Protection, and Intervention**

MARY CASTLE WHITE, RN, MPH, PhD

From the University of California, San Francisco, California.

CORRESPONDENCE

178 **Cigarette Smoking Prevention—Physicians Should Teach by Example**

TSUNG O. CHENG, MD

From the Division of Cardiology, George Washington University, Washington, DC.

178 **Drs Pérez-Stable and Fuentes-Afflick Respond**

ELISEO J. PÉREZ-STABLE, MD and ELENA FUENTES-AFFLICK, MD

From the University of California, San Francisco, California.

OTHER FEATURES

132 **Continuing Medical Education Activities**

179 **Poetry**

182 **Classified Advertising**

185 **Instructions for Authors**

★ Official Journal of the Alaska State Medical Association, the Arizona Medical Association, the California Medical Association, the Denver Medical Society, the Idaho Medical Association, the Nevada State Medical Association, the New Mexico Medical Society, the Utah Medical Association, the Washington State Medical Association, and the Wyoming Medical Society.

Continuing Medical Education

ARIZONA • CALIFORNIA, HAWAII, NEVADA • COLORADO • IDAHO • NEW MEXICO • UTAH • WASHINGTON • WYOMING

ARIZONA

All courses listed have been certified as meeting the criteria for Category I of the ArMA CME Certificate and the AMA Physicians Recognition Award. To list Category I CME programs, please send information to Arizona Medical Association, 810 West Bethany Home Road, Phoenix, AZ 85013; or phone (602) 246-8901.

Brochures and registration forms are available from the contact person or organization sponsoring the program.

October 29–31, 1999—**Neurology for the Non-Neurologist.** The Phoenician, Scottsdale, AZ. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; (800) 421-3756; Fax (303)798-5731.

December 10–12, 1999—**Managing Respiratory Disease.** The Phoenician, Scottsdale, AZ. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; (800) 421-3756; Fax (303)798-5731.

CONTACT INFORMATION

Mayo Clinic-Scottsdale—Contact: Postgraduate Courses, Mayo Clinic-Scottsdale, (602) 301-7447.

U of A—Contact: University of Arizona College of Medicine, Arizona Health Sciences Center, Tucson, AZ 85724. (520) 626-7832; (800) 328-5868.

CALIFORNIA, HAWAII, AND NEVADA

All courses and meetings listed are approved for Category I credit toward the CMA Certificate in CME. To list accredited courses here, please send information at least two months in advance to Paulette Richardson, Continuing Medical Education, California Medical Association, PO Box 7690, San Francisco 94120-7690; or phone (415) 882-3387. For more information on accreditation or certification, please write to the above address.

ALLERGY/IMMUNIZATION

August 13–15, 1999—**A Midsummer Night's Wheeze.** California Society of Allergy, Asthma and Immunology at La Costa Resort and Spa, Carlsbad, CA. 12 hrs. $145-$199. Contact: CSAAI Conference Management at (714) 828-8022.

ANESTHESIOLOGY

November 5–7, 1999—**11th Annual Anesthesiology Update.** Monterey Plaza, Monterey, California. Contact (916) 734-5390.

CARDIOLOGY

March 24–26, 1999—**Coronary Heart Disease Update.** Maui, HI; July 30–August 1, 1999–Yosemite, CA; November 19–21, 1999–Las Vegas, NV. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569 (800) 421-3756 Fax (303)798-5731.

April 17, 1999—**Primary Care Cardiology.** UC Davis at Cancer Center Auditorium, Sacramento, CA. Sat. Contact: UCD (916) 734-5390.

DERMATOLOGY

May 23–26, 1999—**Practical Dermatology for the Primary Care Physician, Las Vegas, NV.** Sponsored by Continuing Medical Education Associates. To be held at the Caesars Palace, Las Vegas, NV. Method: AV, L, SB, W. 20 hrs credit: AMA, AOA, AAFP. $575. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

March 12–14, **1999—Dermatology for the Non-Dermatologist.** Las Vegas, NV; April 23–25, 1999–San Francisco, CA; June 25–27, 1999–Anaheim, CA; September 24–26, 1999–Las Vegas, NV. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, MER,1500 West Canal Court, Suite 500, Littleton, CO 80120-4569 (800)421-3756 Fax (303)798-5731.

EMERGENCY MEDICINE

April 12–13, 1999—**High Risk Emergency Medicine.** Harrah's, Las Vegas, NV. Contact: CEME, 5330 Primrose Drive, Suite 250, Fair Oaks, CA 95628. (800) 651-2363.

May 6–7, 1999—**Challenges in Pediatric Emergency Medicine.** Harrah's, Las Vegas, NV. Contact: CEME, 5330 Primrose Drive, Suite 250, Fair Oaks, CA 95628. (800) 651-2363.

May 13–16, 1999—**Outdoor Emergency Medicine, Scottsdale, AZ.** Sponsored by Continuing Medical Education Associates. Marriott Camelback Inn, Scottsdale, AZ. Method: AV, L, SB, W. 32 hrs credit: AMA, AOA, AAFP. $750. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

May 20–21, 1999—**High Risk Emergency Medicine.** Harrah's, Las Vegas, NV. Contact: CEME, 5330 Primrose Drive, Suite 250, Fair Oaks, CA 95628. (800) 651-2363.

June 3–4, 1999—**Improving Emergency Department Patient Satisfaction and Reducing Length of Stay**. Holiday Inn Chicago City Centre, Chicago, IL. Contact: CEME, 5330 Primrose Drive, Suite 250, Fair Oaks, CA 95628. (800) 651-2363.

August 16–19, 1999—**National Emergency Medicine Board Review.** American College of Emergency Physicians at Harrah's Las Vegas, NV. Mon–Thurs. 40 hrs. $895. Contact: Center for Emergency Medical Education (800) 651-CEME (2363).

ENDOCRINOLOGY

October 22–24, 1999—**Clinical Endocrinology for Primary Care Physicians.** Tropicana, Las Vegas, NV. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; (800) 421-3756, Fax (303)798-5731.

ETHICS

September 22-25, 1999—**Legal Issues in Damaged Brain Injury Cases.** UC Davis at Westin St. Francis Hotel, San Francisco, CA. Contact: UCD (916) 734-5390.

FAMILY PRACTICE/PRIMARY CARE

March 12-14, 1999—**Dermatology for the Non-Dermatologist.** Medical Education Resources at Riviera Hotel and Casino, Las Vegas, NV. 11 hrs. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Ct., Ste. 500, Littleton, CO 80120-4569; (800) 421-3756.

March 21-23, 1999—**Arrhythmias: Interpretation, Diagnosis & Management.** Medical Education Resources at Westin Maui Resort, Maui, HI. 11 hrs. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Ct., Ste. 500, Littleton, CO 80120-4569; (800) 421-3756.

March 27, 1999—**Primary Care Gastroenterology.** UC Davis at Cancer Center Auditorium, Sacramento, CA. Saturday. Contact: UCD (916) 734-5390.

April 23-25, 1999—**Dermatology for the Non-Dermatologist.** Medical Education Resources at Parc Fifty Five, San Francisco, CA. 11 hrs. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Ct., Ste. 500, Littleton, CO 80120-4569; (800) 421-3756.

April 23-25, 1999—**Managing Respiratory Diseases.** Medical Education Resources at Bally's Las Vegas, NV. 11 hrs. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Ct., Ste. 500, Littleton, CO 80120-4569; (800) 421-3756.

April 28, 1999—**Mangement of Benign Uterine Conditions.** UC Davis at Cancer Center Auditorium, Sacramento, CA. 4 hrs. $50. Contact: UCD (916) 734-5390.

May 14-16, 1999—**Neurology for the Non-Neurologist**. Medical Education Resources at Bally's Las Vegas, NV. 11 hrs. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Ct., Ste. 500, Littleton, CO 80120-4569; (800) 421-3756.

May 14–18, 1999—**Primary Care Essentials, San Francisco, CA.** Sponsored by Continuing Medical Education Associates. Grand Hyatt on Union Square, San Francisco, CA. Method: AV, L, SB, W. 32 hrs credit: AMA, AOA, AAFP. $750. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

May 23–26, 1999—**Office Orthopedics and Bone Radiology for the Primary Care Physician.** CMEA at Caesar's Palace, Las Vegas, NV. Sun–Wed, 20 hrs, $575. Contact: Victoria Gonzalez, P.O. Box 270469, San Diego, CA 92198; (800) 993-2632 or (619) 674-5200.

May 23–26, 1999—**Practical Dermatology for the Primary Care Physician.** CMEA at Caesar's Palace, Las Vegas, NV 20 hrs. $575. Contact: Victoria Gonzalez, P.O. Box 270469, San Diego, CA 92198; (800) 993-2632 or (619) 674-5200.

June 5–7, 1999—**8th Annual Primary Care Treatment of Pain.** UC Davis at Tenaya Lodge at Yosemite Fish Camp, CA. Contact: UCD (916) 734-5390

June 13–18, 1999—**23rd Annual Fingers to the Toes Primary Care Orthopaedics.** UC Davis at Stanford Sierra Camp, near South Lake Tahoe. Contact: UCD (916) 734-5390

June 25-27, 1999—**Dermatology for the Non-Dermatologist.** Medical Education Resources at the Hyatt Regency Alicante, Anaheim, CA. 11 hrs. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Ct., Ste. 500, Littleton, CO 80120-4569; (800) 421-3756.

July 5–8, 1999—**Family Practice Board Review Course.** UCSF at Fairmont Hotel, San Francisco, CA. 25 hrs. $525–$575. Contact: Program Coordinator, Dept. Family and Community Medicine, 500 Parnassus Ave, MU-3E, SF, CA 94143-0900 or phone (415) 476-5250.

July 25–29, 1999—**19th Annual Current Concepts in Primary Care Cardiology.** UC Davis at Granlibakken Conference Center, Tahoe City, CA. Contact: UCD (916) 734-5390.

July 30–Aug 1, 1999—**Coronary Heart Disease Update.** Medical Education Resources at Tenaya Lodge, Yosemite, CA. 11 hrs. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Ct., Ste. 500, Littleton, CO 80120-4569; (800) 421-3756.

August 6-8, 1999—**Managing Respiratory Diseases.** Medical Education Resources at the Hyatt Regency Monterey, CA. 11 hrs. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Ct., Ste. 500, Littleton, CO 80120-4569; (800) 421-3756.

INFECTIOUS DISEASE

March 25, April 1, 8, 15, 1999—**Epidemiology and Prevention of Vaccine-Preventable Diseases.** California Distance Learning Health Network. Contact: CDLHN (619) 594-3348.

INTERNAL MEDICINE

March 19–25, 1999—**Internal Medicine, San Diego CA.** Sponsored by Continuing Medical Education Associates. Hotel del Coronado, San Diego, CA. Method: AV, L, SB, W. 45 hrs credit: AMA, AOA, AAFP. $895. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

August 22–27, 1999—**New Advances in Internal Medicine.** UC Davis at Embassy Suites, Monterey, CA. Contact UCD (916) 734-5390.

KEY TO ABBREVIATIONS

DREW:	Charles R. Drew Postgraduate Medical School, Office of Continuing Medical Education, (213) 563-4800.
LLU:	Loma Linda University, Continuing Medical Education Programs, (909) 824-4963.
STAN:	Stanford University, Postgraduate Education, (415) 723-5594.
UCD:	University of California, Davis, Office of Continuing Medical Education, (916) 734-5390.
UCI:	University of California, Irvine, Memorial/UCI Center for Health Education, (714) 824-5926.
UCLA:	University of California, Los Angeles, Continuing Education in Medicine and Health Sciences, (310) 794-2620.
UCSD:	University of California, San Diego, Office of Continuing Medical Education, (619) 534-3940.
UCSF:	University of California, San Francisco, Extended Programs in Medical Education, (415) 476-4251.
USC:	University of Southern California, Postgraduate Division, (800) USC-1119.

NEUROLOGY

May 14–16, 1999—**Neurology for the Non-Neurologist.** Bally's, Las Vegas, NV. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; (800);421-3756; Fax (303)798-5731.

OB/GYN

April 28, 1999—**Mangement of Benign Uterine Conditions.** UC Davis at Cancer Center Auditorium, Sacramento, CA. 4 hrs. $50. Contact: UCD (916) 734-5390.

September 25–26, 1999—**Ultrasound Update: 1999.** Hilton Hotel, Sacramento, CA. (916) 734-5390.

December 10–12, 1999—**Issues in Women's Health.** Tropicana, Las Vegas, NV. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; (800) 421-3756; Fax (303)798-5731.

OCCUPATIONAL & ENVIRONMENTAL

May 14–15, 1999—**Occupational and Environmental Medicine: 1999.** UC Davis at Cancer Center Auditorium, Sacramento, CA. Contact: UCD at (916) 734-5390.

August 5-6, 1999—**Occupational & Environmental Toxicology for the Health & Safety Professional.** UC Berkeley. Holiday Inn Bay Bridge, Emeryville, CA. Contact: Center for Occupational & Environmental Health, UC Berkeley, Richmond Field Station, 1301 S. 46th St., Bldg. 102, Richmond CA 94804; (510) 231-5645; http://socrates.berkeley.edu/~coehce/.

OPHTHALMOLOGY

May 21, 1999—**UC Davis Annual Ophthalmology Symposium.** UC Davis at the Hilton Hotel, Sacramento, CA. Contact: UCD (916) 734-5390.

ORTHOPEDICS

April 10, 1999—**Primary Care Orthopedics, Lower Extremities.** UC Davis at Holiday Inn Northeast, Sacramento, CA. Contact: UCD (916) 734-5390.

June 13–18, 1999—**23rd Annual Fingers to the Toes Primary Care Orthopaedics**. Stanford Sierra Camp, near South Lake Tahoe, Fallen Leaf Lake, CA. Contact (916) 734-5390.

PEDIATRICS

March 12, 1999—**Early Adolescents: How to Save Their Lives.** California Dept. of Health Services at Interactive Satellite Presentations. Contact CDLHN (619) 594-3348.

March 19–20, 1999—**Pediatrics Update: 1999.** UC Davis at Cancer Center Auditorium, Sacramento, CA. Contact: UCD (916) 734-5390.

May 6–8, 1999—**Advances and Controversies in Clinical Pediatrics.** UCSF at Ritz-Carlton Hotel on Nob Hill, San Francisco, CA. Contact: UCSF (415) 476-5808 or Fax (415) 502-1795.

May 17–19, 1999—**18th Annual Conference on Child Abuse and Neglect.** UC Davis at the Radisson Hotel, Sacramento, CA. 21 hrs. $195. Contact: UCD at (916) 734-5390.

June 4-7, 1999—**Pediatric Environmental Health: Putting It Into Practice.** Children's Environmental Health Network. Westin St. Francis, San Francisco, CA. $250-350. Contact Children's Environmental Health Network, (510) 597-1393 x 14 or cehn@cehn.org.

July 16–17,1999—**Seventh Annual Pediatric Update.** Sponsored by Lucile Packard Children's Health Services at Stanford and faculty from UCSF and Stanford Schools of Medicine. Lucile Packard Children's Hospital. Contact: Elinor Meyer, Continuing Medical Education and Physician Relations Department, Lucile Packard Children's Hospital, 725 Welch Road, Palo Alto,CA 94304 (650) 497-8554.

PLASTIC SURGERY

March 18–20, 1999—**11th Annual Symposium on Aesthetic Surgery.** UCSF at Palace Hotel, San Francisco, CA. 19.5 hrs. $950. Contact UCSF (415) 476-5808.

PRIMARY CARE

March 27, 1999—**Primary Care Gastroenterology.** UCDMC, Cancer Center Auditorium, Sacramento, CA. (916) 734-5390.

April 10, 1999—**Primary Care Orthopedics, Lower Extremities.** Holiday Inn Northeast, Sacramento, CA. (916) 734-5390.

April 17, 1999—**Primary Care Cardiology.** UCDMC, Cancer Center Auditorium, Sacramento, CA. (916) 734-5390.

June 5–7, 1999—**8th Annual Primary Care Treatment of Pain.** Tenaya Lodge at Yosemite, Fish Camp, CA. (916) 734-5390.

July 25–29, 1999—**19th Annual Current Concepts in Primary Care Cardiology.** Granlibakken Conference Center, Tahoe City, CA. (916) 734-5390.

October 22–24, 1999. **Clinical Endocrinology for Primary Care Physicians.** Tropicana, Las Vegas, NV. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; (800) 421-3756; Fax (303) 798-5731.

PSYCHIATRY

April 10, 1999—**Psychiatry Update.** UC Davis at Cancer Center Auditorium, Sacramento, CA. Contact: UCD (916) 734-5390.

RADIOLOGY

September 25-26, 1999—**Ultrasound Update: 1999.** UC Davis at Hilton Hotel, Sacramento, CA. Contact: UCD (916) 734-5390.

RESPIRATORY

March 19–20, 1999—**Cystic Fibrosis Caregivers Symposium.** UC Davis at Marriott Hotel, Napa, CA. Contact: UCD (916) 734-5390.

Managing Respiratory Disease–April 23–25, 1999–Las Vegas, NV; June 11–13, 1999–San Francisco, CA; August 6–8, 1999–Monterey, CA. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569 (800)421-3756 Fax (303)798-5731.

SURGERY

April 24, 1999—**3rd Annual Organ Transplant Conference.** UCD at Cancer Center Auditorium, Sacramento, CA. Contact UCD (916) 734-5390.

May 27–29, 1999—**2nd Annual Current Issues in Anatomic Pathology –1999.** UCSF at Mark Hopkins Intercontinental Hotel, SF. 19.5 hrs. $595. Contact: UCSF (415) 476-5808.

GENERAL/MULTIDISCIPLINARY

April 23–25, 1999—**Physician Leadership Program.** California Academy of Family Physicians at Claremont Hotel, Berkeley, CA. 20 hrs. $1245–$1395. Contact: Laura Johnson Morasch (415) 394-9121. Web: www.familydocs.org/Orgs?hcli.html E-mail: HCLI@familydocs.org.

April 28–May 8, 1999—**Blue Water Medical Seminar.** Tri City Medical Center at Baja California aboard Royal Star Sportfisher. 20 hrs. $3300. Contact: Ronald Medak (760) 727-7863.

May 16–19, 1999—**Alternative Medicine, Scottsdale, AZ.** Sponsored by Continuing Medical Education Associates. Marriott Camelback Inn, Scottsdale, AZ. Method: AV, L, SB, W. 20 hrs credit: AMA, AOA, AAFP. $575. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

May 25 & 26, 1999—**BLS Instructor Course.** American Heart Association at San Leandro, CA. 11 hrs. $120. Contact: CPR Seminar (925) 754-7900.

June 22–29, 1999—**Wellness in Practice: Mindfulness-Based Stress Reduction in Mind/Body Medicine.** Enloe Medical Center at Mana L'ea Retreat Center, Maui. Contact: Maui Stress Reduction Retreats, Steve (530) 898-1495.

August 24–25, 1999—**BLS Instructor Course.** American Heart Association at San Leandro. 11 hrs. Contact: CPR Seminars (925) 754-7900.

October 15–17, 1999—**Physician Leadership Program.** California Academy of Family Physicians at Laurel Heights Conference Center, SF. 20 hrs. $1245–$1395. Contact: Laura Johnson Morasch (415) 394-9121. Web: www.familydocs.org/ Orgs?hcli.html (e-mail: HCLI@familydocs.org).

GENERAL

Converse in Spanish—April 9-12, 1999: Glendale Adventist Med Ctr, Los Angeles; May 7-10, 1999: San Francisco; July 9-12, 1999: Scripps Memorial, San Diego; August 13-16, 1999: Sacramento. 36 hrs. $695. Contact: Rios Associates (619) 218-4875.

LOSS PREVENTION

September 22–25, 1999—**Legal Issues in Damaged Brain Injury Cases.** Westin St. Francis Hotel, San Francisco, CA. Contact (916) 734-5390.

HOME STUDY/SELF ASSESSMENT

California Physicians' Legal Handbook Series. California Medical Association. Contact: CMA, P.O. Box 7690, San Francisco 94120-7690. (800) 882-1262.

Breast Cancer, Early Detection and Control. Texas Medical Association. CD ROM. $70. 2 hrs. Contact: Texas Medical Association, (800) 880-1300; http://www.texmed.org/health_science/hs_poep.html

COLORADO

To list CME programs here, please send information at least two months in advance to: Mr Robert L. Kennedy, Denver Medical Society, 1850 Williams Street, Denver, CO 80218; or telephone (303) 377-1850. Brochures, course information, and registration forms are available from the contact person or organization.

Tuesday Noon Conferences—**Various Topics in Medicine.** Lutheran Medical Center, Wheat Ridge. Contact: Jean A. Kline, (303) 425-2951.

First Wednesday of Each Month—**Various Topics in Neurology.** Colorado Society of Clinical Neurologists. Contact: Colorado Society of Neurologists, (303) 449-3566.

Second Wednesday of Each Month—**Cardiovascular Education Series.** St Anthony Hospital at St Anthony Hospital, Denver. Contact: Rose Powell, (303) 629-3678.

March 25–27, 1999—**Neurology For The Non-Neurologist.** Grand Beach Resort, St. Thomas, USVI. Fee $375. Contact Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

March 25–27, 1999—**Clinical Endocrinology For Primary Care Physicans.** Marriott's Beach Resort, St. Grand Cayman. Fee $375. Contact Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

March 26–28, 1999—**Managing Respiratory Diseases.** Buena Vista Palace, Orlando,FL. Fee $375. Contact Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

April 8–10, 1999—**Coronary Heart Disease Update.** Hyatt Regency, Aruba. Fee $375. Contact Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

April 8–10, 1999—**Clinical Endocrinology For Primary Care Physicans.** The Westin Resort, St John, USVI. Fee $375. Contact Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

April 9–11, 1999—**Arrhythmias: Interpretation, Diagnosis & Management.** Hilton Tapatio Cliffs, Scottsdale, AZ. Fee $375. Contact Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

April 9–11, 1999—**Neurology For The Non-Neurologist.** Marriott's Casa Marina, Key West, FL. Fee $375. Contact Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

April 30–May 2, 1999—**Dermatology For The Non-Dermatologist.** South Sea Plantation, Captiva Island, FL. Fee $375. Contact Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

April 30–May 2, 1999—**Clinical Endocrinology For Primary Care Physicans.** Hyatt Regency, New Orleans, LA. Fee $375. Contact Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

May 14–16, 1999—**Managing Respiratory Diseases.** Hilton Resort, Hilton Head, SC. Fee $375. Contact Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

June 17-19, 1999—**Issues in Women's Health.** Hyatt Regency, Grand Cayman. Contact Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

June 18-20, 1999—**Neurology For The Non-Neurologist.** Buena Vista Palace, Orlando, FL. Fee $375. Contact Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

June 24-26, 1999—**Clinical Endocrinology For Primary Care Physicans.** Sonesta Beach Resort, Bermuda. Fee $375. Contact Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

June 25-27, 1999—**Coronary Heart Disease Update.** Sheraton Fiesta Beach Resort, S. Padre Island, TX. Fee $375. Contact Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

CONTACT INFORMATION

U of Colo—Contact: University of Colorado Health Sciences Center, School of Medicine, Office of Continuing Medical Education, 4200 E 9th Ave, Denver 80262. (303) 372-9050 or (800) 882-9153; Fax (303) 372-9065.

IDAHO

To list CME programs here, please send information at least two months in advance to: Ada County Medical Society, Inc. 305 W. Jefferson, PO Box 2668, Boise, Idaho 83701. (208) 336-2930. Brochures, course information, and registration forms are available from the contact person or organization.

NEW MEXICO

Information, requests for accreditation, and items to be listed should be sent to the chair of the CME Committee, New Mexico Medical Society, 7770 Jefferson, Suite 400, Albuquerque, NM87109, at least two months in advance. For information on CME accreditation or on the CME requirements of the New Mexico Board of Medical Examiners, please write to the above address or call (505) 828-0237.

NOTE: Course information in the following listing is subject to change on occasion. Check with the sponsoring institution for current details.

Every First and Third Tuesday—**Building and Implementing Clinical Practice Guidelines at the Point of Care.** Contact: Thomas A. Naegele, DO, (505) 275-7267.

April 28–30, 1999—**The Fourth Annual Clinical Cardiology Management and Diagnostic Dilemmas.** Eldorado Hotel, Santa Fe, NM. 17 Category 1 AMA. Contact: Registration Secretary, American College of Cardiology, 9111 Old Georgetown Rd, Bethesda, MD 20814-1699 (800) 253-4636, ext. 695.

July 30–August 1, 1999–**Neurology for the Non-Neurologist.** Eldorado Hotel, Sante Fe, NM. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; (800) 421-3756; Fax (303)798-5731.

SATELLITE COURSES

Contact: Joe Treat or Jim Cato, Immunization Program, (505) 827-2366.

CONTACT INFORMATION

UNMSOM—University of New Mexico School of Medicine, Office of CME, PO Box 713, Albuquerque 87131. (505) 277-3942.

UTAH

All courses listed meet the criteria for Category 1 of the Physician's Recognition Award of the AMA. To list AMA Category 1 CME courses, send information at least two months in advance to the Office of Continuing Medical Education, 540 East Fifth South, Salt Lake City, UT 84102; or phone (801) 355-7477. For information on CME accreditation, please write the CME office at the above address. NOTE: Course information in the following listing is subject to change on occasion. Check with the sponsoring institution.

MEDICAL GRAND ROUNDS

Weekly—**Grand Rounds in Internal Medicine, Psychiatry, OB/GYN, and Pediatrics.** Contact: UUSM.

Weekly—**Pediatric Grand Rounds.** Contact: PCMC.

WASHINGTON

The listing of continuing medical education programs in Washington state is compiled by the Washington State Medical Association. To list Category 1 programs here, please send information at least two months in advance to Continuing Medical Education, Washington State Medical Association, 2033 Sixth Avenue, Suite 1100, Seattle, WA98121; or phone (206) 441-9762 or (800) 552-0612.

Brochures and registration forms are available from the contact person or organization listed at the end of each course or in the list of course sponsors and contact information.

COURSE SPONSORS AND CONTACT INFORMATION

CME HARBORVIEW—Contact: Gayle Splater, Cytology Continuing Education, Dept. of Pathology, Harborview Medical Center, 325 Ninth Ave, Seattle, WA98104. (206) 223-5953.

PCMS CME—Contact:Executive Director, College of Medical Education, 705 S Ninth, No. 203, Tacoma, WA 98405. (206) 627-7137.

U/W (UNIVERSITY OF WASHINGTON)—Contact: U/W School of Medicine, Div. of CME, SC-50, Seattle, WA98195. (206) 543-1050.

VMMC (VIRGINIA MASON MEDICAL CENTER)—Contact: Linda Orgel, Division of Continuing Medical Education, Virginia Mason Medical Center, POBox 900, Seattle, WA 98111. (206) 340-2058.

WSMA—Washington State Medical Association, Continuing Medical Education, 2033 Sixth Ave, Ste 1100, Seattle, WA 98121. (206) 441-9762.

WYOMING

All courses meet the criteria for Category 1 of the Physician's Recognition Award of the AMA. To list AMA Caegory 1 CME courses here, send information at least two months in advance to the Medical Education Committee, Wyoming Medical Society, P.O. B ox 4009, Cheyenne, WY 82009; email skeefe@wyomed.org; phone 307 634-2424; Fax 307 632-1973.

June 16-18, 1999—**Annual Meeting/Scientific Session: Wyoming Medical Society.** Jackson Lake Lodge, Moran WY. Contact: Susie Wacker, P.O. Box 4009, Cheyenne, WY 82003 or swacker@wyomed.org.

OTHER CME OPPORTUNITIES

Brochures and registration forms are available from the contact person or organization listed at the end of each course or in the list of course sponsors and contact information.

April 17-20, 1999—**Spring Session, American Association of Pediatrics.** Hyatt Regency Chicago, Chicago, IL. Contact: AAP Div of Public Relations, P.O. Box 927, Elk Grove Village, IL 60009-0927; (847) 981-7877; Fax (847) 228-5011.

April 22-25, 1999—**80th Annual Session-American College of Physicians-American Society of Internal Medicine.** Ernest N. Morial Convention Center, New Orleans. Credit 29 hrs. Contact: ACP-ASIM Customer Service (800) 523-1546, ext. 2600; www.acponline.org.

April 23-28, 1999—**American Lung Association/American Thoracic Society International Conference.** San Diego, CA. Contact: ALA/ATS International Conference, 1740 Broadway, New York, NY 10019-4374, or fax ATS at (212) 315-6498.

April 23-30, 1999—**58th Annual American Occupational Health Conference.** Ernest N. Morial Convention Center, New Orleans, LA. Contact: ACOEM Education Dept., 55 W. Seeger Road, Arlington Heights, IL 60005; (847) 228-6850 or Fax (847) 228-1856; www.acoem.org.

April 28-May 2, 1999—**32nd Annual Spring Conference.** Sheraton Seattle Hotel & Towers, Seattle, Washington. Contact: Ray Rosetta, Meetings and Programs Director, Society of Teachers of Family Medicine, 8880 Ward Parkway, Kansas City, MO 64114. Phone (800) 274-2237, ext. 4512.

May 14, 1999—**Setting a New Standard of Care: An Office-Based Management Program for Hyperlipidemia in a Managed Care Environment.** National Association of Managed Care Physicians. Hyatt Crystal City, Arlington, VA. Contact: National Association of Managed Care Physicians. (804) 527-1905.

NOTICE

State Associations should send their CME listings for publication to:

Catherine Nancarrow, Editorial Manager
The Western Journal of Medicine
P.O. Box 7690
San Francisco, CA 94120-7690

(415) 974-5977 • Fax (415) 882-3379

Articles

Effect of Incentives on the Use of Indicated Services in Managed Care

STEVEN Z. PANTILAT, MD; MARGARET CHESNEY, PhD; BERNARD LO, MD; *San Francisco, California*

In managed care, financial incentives and utilization review create conflicts of interest for physicians. We sought to determine whether these incentives would lead physicians to deny indicated services. We surveyed internists practicing in areas with at least 30% penetration of managed care. Our questionnaire included four scenarios in which a test or referral is indicated according to clearly established practice guidelines. We randomly assigned physicians to receive one of five versions of the questionnaire, which differed only in the type of reimbursement incentive and utilization review that applied to the scenarios. We received responses from 710 (70%) of 1,009 internists. Although physicians underutilized services regardless of incentives in all scenarios, physicians whose questionnaires depicted full capitation said that they would order fewer services than physicians whose questionnaires depicted fee-for-service. In the scenario in which an x-ray of the lumbosacral spine is indicated for a patient with low back pain, 86% of physicians randomized to the full capitation version said that they would order the test compared to 94% in the fee-for-service version. Similarly, physicians randomized to scenarios requiring utilization review said that they would order fewer services than those randomized to scenarios requiring completion of an insurance form. Scenarios depicting managed care incentives caused consistent, modest underutilization compared to fee-for-service scenarioes, although physicians underutilized services under all financial incentives and utilization review. In response, physicians must develop better methods for detecting underutilization and devise programs to increase the provision of indicated services.

(Pantilat SZ, Chesney M, Lo B. Effect of incentives on the use of indicated services in managed care. West J Med 1999; 170:137–142)

Managed care has grown in response to rising health care expenditures under fee-for-service reimbursement. In managed care, financial incentives and utilization review encourage physicians to decrease services. These incentives and utilization review affect physician behavior and have resulted in lower utilization of health care services in managed care.[1–4] One concern is that such incentives and utilization review may not differentiate between services that are unindicated and those that are clearly indicated. Incentives that decrease unindicated services benefit patients and promote quality care. Incentives and utilization review under managed care that lead physicians to withhold clearly indicated services create serious ethical conflicts, however, and result in poorer quality of care. Specifically, these incentives create conflicts of interest for physicians and raise concerns that in response to these incentives, physicians may withhold indicated services.[5,6] Furthermore, such conflicts of interest may erode patient trust in physicians.

Comparisons of the quality of care between managed care and fee-for-service settings find equivocal and inconsistent results.[7] Little rigorous, empirical evidence exists, however, to evaluate whether capitation and utilization review lead physicians to withhold clearly indicated medical services. We sought to determine whether financial incentives and utilization review in managed care lead physicians to withhold services that are indicated according to well-established practice guidelines. We examined scenarios in which services were clearly indicated because these situations raise the strongest ethical concerns regarding harm to patients. To define indicated services, we used evidence-based guidelines published in the medical literature, and we asked about clinical scenarios that fell clearly within these guidelines.

From the Division of General Internal Medicine, Department of Medicine, University of California, San Francisco, California, (Drs Pantilat, Chesney, and Lo), the Program in Medical Ethics, University of California, San Francisco, California (Drs Pantilat and Lo), and the Center for AIDS Prevention Studies, University of California, San Francisco, California (Drs Chesney and Lo).

This paper was presented at the Society of General Internal Medicine National Meeting on May 3, 1996.

Reprint requests to Steven Pantilat, MD, 521 Parnassus Avenue, Suite C-126, UCSF, Box 0903, San Francisco, CA 94143-0903.

TABLE 1.—*Case Scenarios and Indicated Tests or Referrals Included in Each Questionnaire*

Case Scenario	*Indicated Test or Referral According to Guideline*
56-year-old woman with 6 weeks of low back pain not responding to conservative therapy with a normal neurologic examination	X-ray of the lumbosacral spine or orthopedic referral to evaluate for cancer or infection[9]
45-year-old woman with atypical angina for two months, no cardiac risk factors and a normal electrocardiogram	Exercise treadmill test to evaluate for significant coronary artery disease[10–13]
46-year-old man with depression unresponsive to two consecutive, 6-week courses of therapeutic dosage of a tricyclic and a selective serotonin reuptake inhibitor antidepressant	Referral to a psychiatrist or other mental health professional for adjunctive psychotherapy[14]
51-year-old woman with epigastric pain of four years duration refractory to H-2 antagonists and treatment for *Helicobacter pylori* with a normal upper gastrointestinal series	Referral to a gastroenterologist for upper endoscopy to evaluate for ulcer or tumor[15–17]

We conducted a randomized questionnaire study of physicians to answer the following research question: "Do financial incentives and utilization review in managed care lead physicians to state that they would deny patients clearly indicated tests and referrals?"

Methods

Subjects

We surveyed internists in the American College of Physicians (ACP) who *1*) self-identified as general internists in group or solo practice primarily involved in patient care and *2*) practice in metropolitan statistical areas with a population greater than 250,000 and at least 30% penetration of managed care.[8] We excluded physicians who primarily conduct research or practice in a group-model health maintenance organization (HMO) or Veterans Affairs, military, or public institution.

Questionnaire

Our questionnaire included four case scenarios in which a test or referral was indicated according to evidence-based guidelines published in the peer reviewed literature (Table 1).[9–17] For each scenario, physicians were asked to indicate whether they would order the test or referral recommended in the guideline and, if not, to write which test or referral they would order, if any. We pretested the scenarios with academic general internists.

Physicians were randomized to receive one of five versions of the questionnaire (Figure 1): These versions differed only in the type of financial incentive and utilization review that applied to all four scenarios. We randomized three types of financial incentives: *1*) fee-for-service, *2*) capitation with a bonus which stated, "assume that each patient has an insurance plan for which you receive a monthly capitation payment with a potential bonus at the end of the year depending on the cost of your referrals and tests", and *3*) full capitation which stated, "assume that each patient has an insurance plan for which you receive a monthly capitation payment from which you pay for all referrals and tests."

We further randomized according to the utilization review that applied to the scenarios. All fee-for-service versions of the questionnaire required completion of an insurance form as the utilization review. The capitation versions were further randomized to two types of utilization review: *1*) review by a committee of colleagues or *2*) preauthorization by telephone. Thus, physicians

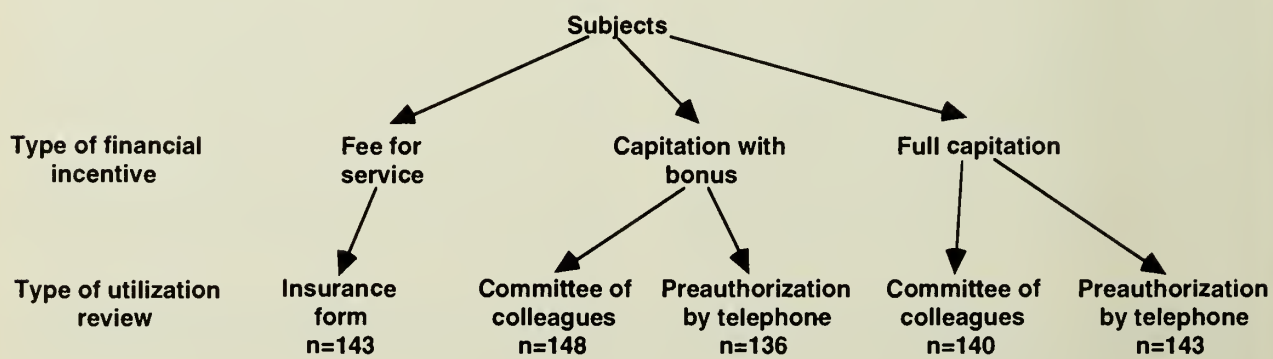


Figure 1.—Randomization to financial incentive and utilization review.

TABLE 2.—*Characteristics of Respondents According to Financial Incentive and Utilization Review Depicted in Questionnaire**

	Fee-for-Service/ Insurance Farm (n = 143)	*Capitation with Banus/ Committee of Colleagues (n = 148)*	*Financial Incentive/ Utilization Review Capitation with Banus/ Preauthorization by Telephone (n = 136)*	*Full Capitation/ Committee of Colleagues (n = 140)*	*Full Capitation/ Preauthorization by Telephone (n = 143)*	*Total Cohort (n = 710)*
Demographics						
Age, y†	46 ± 10	49 ± 11	46 ± 12	48 ± 12	48 ± 11	47 ± 11
Male, %	83	89	85	84	86	85
White, %	80	84	81	79	79	83
Practice characteristics						
Experience with managed care, h/wk†	6 ± 5	7 ± 6	6 ± 5	6 ± 6	6 ± 5	6 ± 5
Patient care, h/wk†	39 ± 14	38 ± 14	38 ± 15	37 ± 14	39 ± 14	38 ± 14
Practice setting, %						
Solo	34	44	40	42	39	40
Group	49	45	48	45	47	47

* There were no statistically signficant differences between groups.
† Values given as the mean ± SD.

were assigned one of five versions of the questionnaire, with each version including the identical case scenario.

Each questionnaire also asked about demographics and practice characteristics.

Our protocol was approved by the University of California, San Francisco Committee on Human Research.

Data Analysis

We recorded the percentage of physicians who stated that they would order the indicated test or referral or who stated that they would order a different test or referral that would achieve the same goal. For the scenario in which the patient with low back pain needs an x-ray of the lumbosacral spine in order to rule out cancer or infection, a referral to an orthopedic surgeon was counted as an appropriate measure because the referral would likely lead to an x-ray of the lumbosacral spine. A computed tomographic (CT) scan or magnetic resonance imaging (MRI) was also counted as an appropriate measure, although referral to physical therapy was not. A treadmill test with thallium or a stress echocardiogram was also scored correct for the patient with atypical angina for whom a treadmill test is indicated. For the scenario in which a referral to a gastroenterologist for upper endoscopy is indicated, we considered any referral to a gastroenterologist or for upper endoscopy correct. For the scenario depicting a man who remains depressed after medical therapy, we considered a referral to any mental health professional correct.

For each scenario, we performed a chi-square test to assess trends in the proportion of physicians who indicated that they would order the test or referral according to the type of financial incentive or utilization review to which they were randomized. We hypothesized that among financial incentives, full capitation would be the most restrictive and fee-for-service the least restrictive. Similarly, we hypothesized that among types of utilization review, preauthorization by telephone would lead physicians to state that they would order the fewest number of indicated tests while completion of an insurance form would lead physicians to indicate that they would order the most. We analyzed the data to examine this predicted trend. We performed all statistical analyses using STATISTICA 4.1 for the Macintosh (StatSoft; Tulsa, OK).

Results

We mailed 1,030 questionnaires and received responses from 710 (70%) of 1,009 eligible subjects. We excluded 21 subjects who moved without leaving a forwarding address, died, or were no longer in practice. Respondents were predominantly white males with busy practices (Table 2). Respondents had experience with managed care, fee-for-service reimbursement (Table 3), capitation, utilization review, preauthorization by telephone, HMO review, and review by a committee of colleagues. Groups of physicians randomized to receive different versions of the questionnaire did not differ significantly in characteristics.

The percentage of physicians stating that they would order an indicated test or referral varied from scenario to scenario (Table 4). The more restrictive the financial incentive, the less likely physicians were to state that they would order the indicated test or referral. In the case of the patient with low back pain, 86% of physicians randomized to full capitation scenarios said that they would order the test, compared to 94% of physicians randomized to fee-for-service scenarios. Among physicians randomized to the full capitation scenario, 51% said that they would order a referral to a gastroenterologist for the patient with dyspepsia, compared to 61% of physicians randomized to fee-for-service scenarios. We found similar, but not statistically significant,

TABLE 3.—*Percent of Physicians who Experience Each Method of Reimbursement and Type of Utilization Review in Their Practice*

	% of Physicians Who Experience Each Type (n = 710)
Reimbursement	
Fee-for-service	90
Discounted fee-for-service	68
Self-pay	68
Any capitation	44
Capitation with bonus	30
Full capitation	27
Other	13
Utilization review	
Preauthorization by telephone	83
Review of tests and referrals by HMO	54
HMO published profile of cost per patient per month	46
Review by a committee of colleagues	31

trends toward fewer services in the other scenarios by physicians randomized to capitation.

Managed care utilization review did not significantly decrease the percentage of physicians who said they would order tests or referrals (Table 5), although a trend in that direction was found. We found no association between physicians stating that they would order the indicated test or referral and their actual experience with utilization review.

We analyzed responses to the scenarios by the combination of incentives to detect any interaction between them (Table 6). For the scenarios in which the trends were statistically significant, only 84% of physicians randomized to the most restrictive managed care scenarios of full capitation and preauthorization by telephone said they would order the indicated x-ray for low back pain, compared to 94% of physicians randomized to fee-for-service scenarios. Only 50% of physicians randomized to the most restrictive scenario said they would refer the patient with dyspepsia for endoscopy compared to 61% of physicians randomized to the least restrictive scenarios.

Discussion

The medical community has shown concern that incentives in managed care will lead physicians to withhold medically indicated services, thereby compromising the quality of care and eroding patient trust.[5,6]

Our survey results suggest this concern is warranted, but should not be overstated. Compared to fee-for-service, capitation and utilization review caused a small but consistent decrease of 3% to 11% in physicians stating that they would order indicated tests and referrals. Because of our study's randomized design, we conclude that this difference, though modest, resulted from the financial incentives and utilization review depicted on our questionnaire, and not from factors such as demographics, practice characteristics, or experience with managed care; all factors were balanced in the randomized groups.

We also found, under various types of financial incentives and utilization review, that many physicians would not order indicated tests and referrals. Even among those physicians randomized to fee-for-service scenarios, 6% to 39% failed to say that they would order the indicated services.

These results provide modest support for the concerns that conflicts of interest may lead physicians to fail to act in their patients' best interests. The incentives used in our study led to only a small amount of underutilization, not gross lapses in the quality of care. Even this level of underutilization, however, matters for patients. For instance, a physician who fails to order an indicated exercise treadmill test for a woman with atypical angina could miss the diagnosis of significant coronary artery disease and fail to prevent a myocardial infarction or death.

Studies of actual practice suggest that our findings may underestimate the true level of underutilization. In a study that closely parallels our scenarios, salaried physicians in a staff-model HMO underutilized x-rays for patients with low back pain by 71%.[18] Adherence to preventive guidelines ranges from 50% for the National Cholesterol Education Program guidelines to 15% to 26% for mammography in an inner-city population.[19,20]

TABLE 4.—*Percent of Physicians Indicating They Would Order the Test or Referral According to Financial Incentive*

	Financial Incentive		
		Capitation with Bonus (n = 283)	
Scenario	Fee-for-Service (n = 141)	%	Full Capitation (n = 278)
X-ray for low back pain*	94	92	86
Stress test for atypical angina	89	84	85
Mental health referral for depression	81	78	78
Gastroenterology referral for dyspepsia†	61	60	51

*$P < .05$
†$P = .02$

TABLE 5.—*Percent of Physicians Indicating They Would Order the Test or Referral According to Utilization Review*

Scenario	Utilization Review: Insurance Form (n = 141)	Committee of Calleagues (n = 283) %	Preauthorization by Telephone (n = 278)
X-ray for low back pain*	94	90	88
Stress test for atypical angina	89	83	86
Mental health referral for depression	81	80	75
Gastroenterology referral for dyspepsia	61	56	55

*P = .06

Several reasons can explain why our findings may not reflect true rates of underutilization and the influence of incentives. Our subjects, ACP members of whom most are board certified in internal medicine, may be more knowledgeable about guidelines than a general sample of primary care physicians. Also, physicians are more likely to say that they would order the test or referral on a questionnaire than in real practice if they realize the "correct" answer.[21,22] A physician's decision regarding a given intervention may be affected by the source of the guideline, the invasiveness of the intervention, the need to involve another physician, and the implications of a missed diagnosis. Although our study was not designed to examine this issue directly, our results suggest that the quality of care might be improved by focusing as much, if not more, attention on encouraging physicians to adhere to reliable guidelines, rather than simply working to eliminate the effects of incentives in managed care. In fact, the level of underutilization we found for fee-for-service scenarios suggests that unless we improve adherence to reliable guidelines in all systems of care, the quality of care may suffer even in systems without any incentives to withhold services.

Our study has several limitations. Our results may not be generalizable to physicians who work in staff-model HMOs or government institutions, or to physicians who practice in areas of low, managed care penetration. We chose areas of the country with at least 30% penetration of managed care to insure that physicians would have at least some exposure and experience with the incentives depicted. Also, using different physicians as a pretest population, different guidelines or different scenarios may have affected our findings.[23]

Conclusions

A major ethical concern about incentives in managed care is that incentives may lead physicians to fail to act in the patient's best interest. Within the limitations of our study, we found some evidence that such incentives may have a small but real influence, leading physicians to withhold indicated services. This excess underutilization, though modest, may undermine patient trust in physicians. We also found that, regardless of incentives, a significant number of physicians failed to state that they would order indicated services. Poor adherence to guidelines also threatens the quality of care. Our findings underscore the need for better methods for detecting underutilization. Programs are also needed to ensure that physicians provide indicated services to their patients. These steps could mitigate ethical concerns regarding incentives, improve the quality of care, and bolster patient trust.

TABLE 6.—*Percent of Physicians Indicating They Would Order the Test or Referral According to Combination of Financial Incentive and Utilization Review*

Scenario	Version: Financial Incentive/Utilization Review: Fee-for-Service/Insurance Form (n = 143)	Copitotian with Banus/Committee of Colleogues (n = 148)	Capitatian with Banus/Preouthorizotion by Telephone (n = 136) %	Full Copitotion/Committee of Calleagues (n = 140)	Full Capitation/Preautharization by Telephone (n = 143)
X-ray for low back pain*	94	92	93	88	84
Stress test for atypical angina	89	83	85	84	85
Mental health referral for depression	81	81	75	81	75
Gastroenterology referral for dyspepsia†	61	59	61	51	50

*P < .005
†P = .03

Acknowledgments

The authors thank Michelle McDermid, Lois Snyder, JD, and Warren Browner, MD, for their help with this project. We also thank all the physicians who participated.

This work was conducted while Dr Pantilat was a participant in the Robert Wood Johnson Clinical Scholars Program at UC San Francisco. This work was supported by the Robert Wood Johnson Foundation, the Walter and Elise Haas Fund, and Center Grant MH 42459 from the National Institute of Mental Health.

REFERENCES

1. Rapoport J, Gehlbach S, Lemeshow S, Teres D. Resource utilization among intensive care patients: managed care vs traditional insurance. Arch Intern Med 1992; 152:2207–2212

2. Murray JP, Greenfield S, Kaplan SH, Yano EM. Ambulatory testing for capitation and fee-for-service patients in the same practice setting: relationship to outcomes. Med Care 1992; 30:252–261

3. Hillman AL. Financial incentives for physicians in HMOs. Is there a conflict of interest? N Engl J Med 1987; 317:1743–1748

4. Hillman AL, Pauly MV, Kerstein JJ. How do financial incentives affect physicians' clinical decisions and the financial performance of health maintenance organizations? N Engl J Med 1989; 321:86–92

5. Angell M. The doctor as double agent. Kennedy Inst Ethics J 1993; 3:279–286

6. Rodwin MA. Conflicts in managed care. N Engl J Med 1995; 332:604–607

7. Miller RH, Luft HS. Does managed care lead to better or worse quality of care? Health Affairs 1997; 16:7–25

8. The InterStudy Competitive Edge. 1994; 4:68–92

9. Agency for Health Care Policy and Research. Acute low back problems in adults—assessment and treatment. Clin Pract Guide Quick Ref Guide Clin 1994; 14:1–25

10. Kotler TS, Diamond GA. Exercise thallium-201 scintigraphy in the diagnosis and prognosis of coronary artery disease. Ann Intern Med 1990; 113:684–702

11. Diamond GA, Forrester JS. Analysis of probability as an aid in the clinical diagnosis of coronary-artery disease. N Engl J Med 1979; 300:1350–1358

12. Pryor DB, Harrell FE, Jr., Lee KL, Califf RM, Rosati RA. Estimating the likelihood of significant coronary artery disease. Am J Med 1983; 75:771–780

13. American College of Physicians. Efficacy of exercise thallium-201 scintigraphy in the diagnosis and prognosis of coronary artery disease. Ann Intern Med 1990; 113:703–704

14. Agency for Health Care Policy and Research. Depression in primary care—guideline overview. J Natl Med Assoc 1993; 85:501–503

15. Kahn KL, Kosecoff J, Chassin MR, Solomon DH, Brook RH. The use and misuse of upper gastrointestinal endoscopy. Ann Intern Med 1988; 109:664–670

16. Health and Public Policy Committee, American College of Physicians. Endoscopy in the evaluation of dyspepsia. Ann Intern Med 1985; 102:266–269

17. NIH Consensus Development Panel on *Helicobacter pylori* in Peptic Ulcer Disease. *Helicobacter pylori* in peptic ulcer disease. NIH Consensus Conference. JAMA 1994; 272:65–69

18. Schroth WS, Schectman JM, Elinsky EG, Panagides JC. Utilization of medical services for the treatment of acute low back pain—conformance with clinical guidelines. J Gen Intern Med 1992; 7:486–491

19. Headrick LA, Speroff T, Pelecanos HI, Cebul RD. Efforts to improve compliance with the National Cholesterol Education Program guidelines. Results of a randomized controlled trial [see comments]. Arch Intern Med 1992;152:2490–2496

20. Burack RC, Gimotty PA, Stengle W, Warbasse L, Moncrease A: Patterns of use of mammography among inner-city Detroit women: contrasts between a health department, HMO, and private hospital. Med Care 1993; 31:322–334

21. Norman GR, Feightner JW. A comparison of behaviour on simulated patients and patient management problems. Med Educ 1981; 15:26–32

22. Holmes MM, Rovner DR, Rothert ML, Schmitt N, Given CW, Ialongo NS. Methods of analyzing physician practice patterns in hypertension. Med Care 1989; 27:59–68

23. Tunis SR, Hayward RS, Wilson MC, et al. Internists' attitudes about clinical practice guidelines [see comments]. Ann Intern Med 1994; 120:956–963

Cluster of Postinjection Abscesses Related to Corticosteroid Injections and Use of Benzalkonium Chloride

REBECCA K. OLSON, PhD, *San Francisco, California*; RONALD E. VOORHEES, MD, MPH; HAROLD E. EITZEN, PhD, *Santa Fe, New Mexico;* HENRY ROLKA, MS, *Atlanta, Georgia;* C. MACK SEWELL, DrPH, MS, *Santa Fe, New Mexico*

Benzalkonium chloride (BC) is an unreliable disinfectant. A matched case–control study and environmental investigation were conducted to determine the cause of and risk factors for a cluster of postinjection abscesses at a private medical clinic where BC was used as a disinfectant. Twenty-eight case-patients who had an abscess at the injection site were matched with 126 control patients who had received an intramuscular injection at the clinic on the same day. Risk factors for abscess development in a multivariable logistic model were corticosteroid injection and being female. All case-patients had received a corticosteroid injection from a multidose vial. Cultures of abscesses from 20 of 23 case-patients grew *Pseudomonas aeruginosa*. Cultures of BC prepared at the clinic also grew *P aeruginosa*, suggesting that BC was the source of infection. Injection site cleaning with BC did not appear to be the route of infection since use of BC at the time of injection was not associated with abscess development. A more likely route of infection was injection of contaminated corticosteroid from multidose vials that could have been inoculated with pseudomonads via needle puncture after vial septa were wiped with contaminated BC. Benzalkonium chloride should not be used to clean injection vial septa or injection sites.

(Olson RK, Voorhees RE, Eitzen HE, Rolka H, Sewell CM. Cluster of postinjection abscesses related to corticosteroid injections and use of benzalkonium chloride. West J Med 1999; 170:143–147)

Benzalkonium chloride is an unreliable disinfectant: Gram-negative organisms (eg, pseudomonads) often are resistant to benzalkonium chloride, and benzalkonium chloride's efficacy is diminished when substances that adsorb the compound (eg, cotton balls or gauze) are immersed in it.[1–3] The use of benzalkonium chloride in hospitals has been discouraged by the Centers for Disease Control and Prevention since 1976.[4]

In spring 1995, several patients at a private medical clinic in New Mexico began complaining of pain and swelling at the injection site after receiving intramuscular (IM) corticosteroid injections. *Pseudomonas aeruginosa* was later cultured from several patients' abscesses, and the clinic discontinued these corticosteroid injections. The clinic had been using cotton balls soaked in alcohol or benzalkonium chloride to clean injection sites and injection-vial septa. The Office of Epidemiology of the New Mexico Department of Health (NMDOH) initiated an investigation to determine whether use of benzalkonium chloride was the cause of this cluster of postinjection abscesses and to identify other risk factors for abscess development among clinic patients.

Methods

Epidemiologic Investigation

We defined a case as a patient with an abscess at the injection site that drained pus spontaneously or surgically following an injection at the clinic during January–June 1995. Case-patients were identified through the clinic, local surgeons, and patients' attorneys.

We conducted a matched case–control study to identify risk factors for postinjection abscess development in patients receiving IM injections at the clinic. Through interviews with case-patients and review of

From the Epidemic Intelligence Service (Dr Olson) and the Division of Prevention Research and Analytic Methods (Mr Rolka), Epidemiology Program Office, Centers for Disease Control and Prevention, Atlanta, Georgia; Office of Epidemiology (Drs Voorhees, Eitzen, and Sewell), New Mexico Department of Health, Santa Fe, New Mexico. Dr Olson is now with California Medical Review, Inc, San Francisco, California; Henry Rolka is now with the National Immunization Program, Centers for Disease Control and Prevention.

Reprint requests to The Western Journal of Medicine, 221 Main Street, San Francisco, CA 94120-7690.

their medical charts, we identified the day on which each of the case-patients received the injection associated with their abscess. All other patients receiving IM injections on those days served as controls. We reviewed medical records and interviewed case- and control-patients using a standard questionnaire. The questionnaire requested information regarding demographic factors, clinical signs and symptoms, and potential risk factors.

The following potential risk factors for abscess formation were assessed: age; sex; body mass index [BMI = weight in kg/(height in m)^2] in adults; presence of selected health conditions that affect the immune response—regular use of steroids, diabetes, chemotherapy or radiation therapy for cancer at the time of the injection, or other immunosuppressive conditions; injection site (gluteal versus deltoid); type of medication received (corticosteroid versus other); type of vial (multidose versus single-dose); individual administering injection; and type of disinfectant used to clean the injection site and injection-vial septum (benzalkonium chloride versus alcohol). The disinfectant used at the time of injection was assumed to be whichever disinfectant the person administering the injection had normally used during the months when case-patients received injections. All intramuscular injections were given by five clinic employees who were very consistent in their use of either benzalkonium chloride or alcohol as a disinfectant during that time period: Four reported using the same disinfectant 100% of the time, and one reported using the same disinfectant 80% of the time.

We calculated odds ratios (ORs) for each risk factor with respect to abscess development in accordance with a frequency matched design in which cases were matched with controls by injection date. Because of small cell sizes for some injection dates, we calculated conditional maximum likelihood estimates of the ORs using an exact estimation approach. We also assessed the independent contribution of risk factors when considered simultaneously in a conditional logistic regression model. The statistical software packages StatXact 3 for Windows and LogXact were used for the statistical analyses.[5,6] Statistical significance was defined as a P value < .05.

The investigation was conducted under the authority of the New Mexico Public Health Act; therefore, approval from an institutional review board was not sought. Consent was obtained from each patient before proceeding with the telephone interview.

Environmental and Laboratory Investigation

We asked clinic staff to prepare a stock solution of benzalkonium chloride in the same manner as was done before its use was discontinued prior to our investigation. Cultures were taken of cotton balls soaked in this solution. Other environmental samples from the clinic were benzalkonium chloride concentrate (17% Zephiran® Chloride), tap water, cotton balls soaked in alcohol, hand washes used by clinic personnel, swabs from the tops of eight opened multidose vials, and samples from the contents of two of these vials. All cultures were performed by NMDOH's Scientific Laboratory Division (SLD) using standard methods.[7,8]

The clinic returned unopened vials of triamcinolone acetonide (TA), the most common corticosteroid used at the clinic, to the manufacturer (Steris Laboratories, Inc, Phoenix, AZ) for sterility testing. An opened vial of TA and 18 opened multidose vials of other injectable medications (eg, estrogen, testosterone, vitamin B_{12}, vaccines) from the clinic were sent to the US Food and Drug Administration (FDA) laboratory in Denver, Colorado for sterility testing.

Laboratory records were obtained for all case-patients whose abscesses were cultured. All available patient isolates were sent to SLD for identification confirmation using standard methods[8] and for further categorization using the Microbial Identification System (MIS), which categorizes isolates based on fatty acid methyl esters of the cell wall.[9] Patient isolates were also sent to the University of New Mexico Health Science Center, Molecular Epidemiology Laboratory for DNA fingerprint analysis using pulse-field gel electrophoresis.[10]

Results

Epidemiologic Investigation

A total of 28 patients met the case definition; none had more than one abscess. The 28 case-patients received the injections associated with their abscesses during a 2-month period (April 20–June 22, 1995). Case-patients ranged in age from 13.6 to 79.8 years (mean = 43.2); 23 (82.1%) were female.

All case-patients had been given a corticosteroid injection to relieve allergy symptoms: Twenty-four (85.7%) received triamcinolone acetonide (TA) (dose range: 30–80 mg), three (10.7%) received methylprednisolone acetate (dose: 80 mg), and for one case-patient, whether TA or triamcinolone diacetate was given could not be determined. For two patients, we could not determine whether the injection of methylprednisolone or another injection given at the same time was the one associated with abscess formation. These case-patients were excluded from analyses involving medication. Abscesses began draining (spontaneously or surgically) a median of 75.5 (range: 32–211) days after the injection. Five (17.9%) case-patients were hospitalized for 1–13 days (median = 2 days).

We interviewed 126 (90%) of the 140 patients who had received IM injections on the same days that case-patients received the injection associated with their abscess. No significant differences with respect to sex, mean age, or proportion receiving a corticosteroid injection existed between the 14 control patients who could not be interviewed and the 126 patients who participated in the study.

When we compared case- and control-patients, abscess formation was not associated with immunosup-

TABLE 1.—*Comparison of Risk Factors for Abscess Formation in Case- and Control-Patients*

Potential Risk Factor	Case		Control		OR*(95% CI)†
	n	%	*n*	%	
Sex: female	28	82.1	126	50.8	5.1 (1.7, 19.2)
BMI‡: ≥30	27	7.4	107	17.8	0.4 (0.0, 1.8)
Site: gluteal	28	100.0	119	82.4	Undef (1.3, Undef)
Medication: corticosteroid	26	100.0	126	48.4	Undef (5.9, Undef)
Type of vial: multidose	28	100.0	126	86.5	Undef (1.2, Undef)
Disinfectant used: BC	25	36.0	107	43.9	0.5 (0.2, 1.5)

BC = benzalkonium chloride, Undef = undefined

*Conditional maximum likelihood estimate of odds ratio; case- and control-patients matched on injection date.
†Exact 95% confidence interval.
‡Body mass index; only calculated for adults.

pressive conditions, age, or the person administering the injection. Being female, corticosteroid injection, injection from a multidose vial, and injection in the gluteal muscle were significantly associated with abscess formation (Table 1). When we adjusted the effects of the risk factors listed in Table 1 with a conditional logistic regression model, the effects of injection site and type of vial were inestimable in the model due to lack of variation between case- and control-patients within too many matched case-control groups. We removed these two risk factors and constructed a model with the remaining variables (Table 2). Only receipt of corticosteroid (OR = 17.8) and being female (OR = 7.4) were significantly associated with abscess formation.

Environmental and Laboratory Investigation

Cultures from cotton balls soaked in the demonstration benzalkonium chloride solution from the clinic grew *P aeruginosa*. The solution was prepared monthly by mixing approximately one part Zephiran® Chloride (17%) and two parts commercial normal saline in a glass canister and adding cotton balls. The canister was washed with soap between batches of benzalkonium chloride. None of the other environmental samples collected from the clinic were contaminated with *P aeruginosa*.

Unopened vials of TA passed standard sterility tests conducted by the manufacturer. The FDA found no evidence of microbial contamination in 1 opened, multidose vial of TA or in the 18 opened, multidose vials of other injectable medications.

The abscesses of 23 case-patients were cultured; laboratory records showed that 20 (87.0%) grew *P aeruginosa*, and one grew *Pseudomonas fluorescens/putida*. We obtained *P aeruginosa* isolates from three case-patients: All isolates were confirmed to be *P aeruginosa* by SLD. Isolates from two patients were identified as the same strain by MIS and pulse-field gel electrophoresis.

Discussion

Contaminated benzalkonium chloride has been implicated as the source of infection in several nosocomial outbreaks over the past 40 years[2,11–16] and was also the most likely source of infection in this cluster of abscesses. Benzalkonium chloride solution from the clinic grew *P aeruginosa* as did the majority of abscesses, whereas other environmental samples and unopened vials of TA were not contaminated. The canister containing benzalkonium chloride solution was not disinfected between batches, and once contaminated, could have contaminated successive batches. Two strains of *P aeruginosa* were identified among three patient isolates and *P putida/fluorescens* was isolated from one patient's abscess, suggesting that the canister may have become contaminated with several *Pseudomonas* strains and species. Unfortunately, the isolate from the benzalkonium chloride solution was discarded before it could be compared with patient isolates.

Contaminated benzalkonium chloride could have led to abscesses in patients via two main pathways. First, use of contaminated benzalkonium chloride solution at the time of injection could have contaminated the hands of the person administering the injection, the skin of the patient at the injection site, and/or the needle used for the injection. Any of these factors could have resulted in infection in patients. Second, the contents of multidose vials could have become contaminated when vial septa were wiped with contaminated benzalkonium chloride and punctured with a needle. Injection of contaminated medication could cause infection, regardless of the disinfectant used at the time of injection. We found that use of benzalkonium chloride on patients at the time of the injection was not a risk factor for abscess development. More than half of the case-patients received injections from clinic personnel who used alcohol to clean injection sites and vial septa. These findings suggest that the first pathway was not a significant contributing factor to infection in patients and that the second pathway (contamination of multidose vials) is a more significant explanation for this cluster of abscesses.

TABLE 2.—*Multivariable Analysis of Risk Factors for Abscess Formation*

Potential Risk Factor	*Adjusted OR**	*Exact 95% CI†*
Sex: female	7.4	1.6–69.1
Body mass index‡: > 30	0.2	0.0–1.3
Medication: corticosteroid	17.7	2.7–undefined
Disinfectant used: BC	0.6	0.1–2.5

BC = benzalkonium chloride

*Conditional maximum likelihood estimate of odds ratio; case- and control-patients matched on injection date.
†Exact 95% confidence interval.
‡Only calculated for adults.

The clinic did not record from which vial each patient received an injection; thus it was impossible to determine whether case-patients were associated only with injections withdrawn from vials that had been wiped previously with benzalkonium chloride. The one opened vial of TA available for testing was not contaminated with *Pseudomonas* spp. The vial may not have been wiped with benzalkonium chloride, however, and the vial was cultured several months after it was opened, allowing sufficient time for any present organisms to have died.

Receiving a corticosteroid injection was a strong risk factor for abscess development in persons receiving IM injections at the clinic (Tables 1 and 2). All case-patients received a corticosteroid injection compared with 48.4% of control-patients. Corticosteroids were the only medication associated with abscess development, although at least nine other medications from multidose vials also were used at the clinic. This outcome may have been due to the immunosuppressive effects of pharmacologic dosages of glucocorticoids (eg, TA and methylprednisolone).[1] Corticosteroid injections have been involved in other nosocomial outbreaks,[15,16] including a cluster of abscesses following IM injection of methylprednisolone in New Mexico in 1978.[17]

All case-patients received corticosteroid injections from multidose vials administered in the gluteal muscle. To try to separate the effects of these highly associated variables, we first limited the analysis to patients receiving medications from multidose vials and then to patients receiving injections in the gluteal muscle only. Corticosteroid injection remained a strong, statistically significant risk factor for abscess development in both of these models (exact 95% confidence interval = [4.18, undefined] and [3.45, undefined], respectively), whereas injection site was no longer significant in the first model, and vial type was no longer significant in the second. These results suggest that corticosteroid injection was the most important risk factor of the three; vial type and injection site may have appeared as risk factors only because of their association with corticosteroid injections.

Being female was a risk factor for postinjection abscess development even when controlling for body mass index in the logistic model. Females also were more likely than males to develop abscesses following injections of methylprednisolone in the 1978 cluster of abscesses in New Mexico mentioned earlier.[17] Reasons for this difference between males and females were not clear.

Although benzalkonium chloride has been documented as a significant nosocomial infection liability for many years, this cluster of abscesses illustrates that some health-care providers remain unaware of the dangers of using it as a disinfectant or skin antiseptic. The use of benzalkonium chloride at this clinic may not be an isolated incident; 12% of respondents of a country-wide survey of hospital epidemiologists reported that benzalkonium chloride was in use for skin disinfection at their hospital.[18] Given the unreliability of benzalkonium chloride as a disinfectant and antiseptic[1–4,11–16] and the availability of more efficacious products,[4] benzalkonium chloride should not be used to clean injection vial septa or the skin of patients before injections. Given the potential for contamination of multidose vials, health care providers should consider using single-dose vials of injectable medications when possible, especially when administering corticosteroids.

Acknowledgments

The authors thank David Espey, MD, Paul Ettestad, DVM, David Keller, MD, Terry Sanchez, Jim Sejvar, MD, and Martha Tanuz, RN, for their help in conducting the case-control study; Kerry Hatch and Linda Nims, MS, for typing and categorizing the patient isolates; Pauline Gutierrez, MS and JoAnna Miller for culturing environmental samples; James C. McLaughlin, PhD and Virginia K. Quenzer, MT, SM, for conducting the pulse-field gel electrophoresis; and Laura Fehrs, MD, for her review of the manuscript.

REFERENCES

1. American Hospital Formulary Service (AHFS) Drug Information. Bethesda, MD, The American Society of Hospital Pharmacists, Inc, 1995

2. Malizia WF, Gangarosa EJ, Goley AF. Benzalkonium chloride as a source of infection. N Engl J Med 1960; 263:800–802

3. Kundsin RB, Walter CW. Investigations on adsorption of benzalkonium chloride U.S.P. by skin, gloves, and sponges. AMA Arch Surg 1957; 75:1036–1042

4. Dixon RE, Kaslow RA, Mackel DC, Fulkerson CC, Mallison GF. Aqueous quaternary ammonium antiseptics and disinfectants: use and misuse. JAMA 1976; 236:2415–2417

5. StatXact 3 for Windows: statistical software for exact nonparametric inference. Cambridge, MA, Cytel Software Corporation, 1995

6. LogXact: logistic regression software featuring exact methods. Cambridge, MA, Cytel Software Corporation, 1993

7. American Public Health Association, American Water Works Association, and Water Environment Federation. Standard Methods for the Examination of Water and Wastewater. 18th ed. Washington, DC, American Public Health Association, 1992

8. Weyant RS, Moss CW, Weaver RE, et al. Identification of Unusual Pathogenic Gram-Negative Aerobic and Facultatively Anaerobic Bacteria. 2nd ed. Baltimore, MD, Williams & Wilkins, 1995

9. Miller LT. Single derivatization method for routine analysis of bacterial whole-cell fatty acid methyl esters, including hydroxy acids. J Clin Microbiol 1982; 16:584–586

10. Maslow JN, Slutsky AM, Arbeit RD. Application of pulse-field gel electrophoresis to molecular epidemiology. In Persing DH, Smith TF, Tenover FC, White TJ, (Eds). Diagnostic Molecular Microbiology; Principles and Applications. Washington, DC, American Society for Microbiology, 1993. pp 563–572

11. Plotkin SA, Austrian R. Bacteremia caused by *Pseudomonas SP* following the use of materials stored in solutions of a cationic surface-active agent. Am J Med Sci 1958; 235:621–627

12. Lee JC, Fialkow PJ. Benzalkonium chloride—source of hospital infection with Gram-negative bacteria. JAMA 1961; 177:708–710

13. Frank MJ, Schaffner W. Contaminated aqueous benzalkonium chloride: an unnecessary hospital infection hazard. JAMA 1976; 236:2418–2419

14. Fox JG, Beaucage CM, Folta CA, Thornton GW. Nosocomial transmission of *Serratia marcescens* in a veterinary hospital due to contamination by henzalkonium chloride. J Clin Microbiol 1981; 14:157–160

15. Sautter, RL, Mattman LH, Legaspi RC. *Serratia marcescens* meningitis associated with a contaminated benzalkonium chloride solution. Infect Control 1984; 5:223–225

16. Nakashima AK, McCarthy MA, Martone WJ, Anderson RL. Epidemic septic arthritis caused by *Serratia marcescens* and associated with a henzalkonium chloride antiseptic. J Clin Microbiol 1987; 25:1014–1018

17. Edell TA. *Serratia marcescens* deep tissue abscesses associated with intramuscular injection of medication [Internal Report]. Atlanta, Ga, Field Services Division and Bacterial Diseases Division, Bureau of Epidemiology, Centers for Disease Control and Prevention, 1979

18. Donowitz LG. Benzalkonium chloride is still in use. Infect Control Hosp Epidemiol 1991; 12:186–187

Articles

Cancer Screening Practices Among Primary Care Physicians Serving Chinese Americans in San Francisco

MARION M. LEE, PhD; FLORENCE LEE, MPH; SUSAN STEWART, PhD; STEPHEN McPHEE, MD
San Francisco, California

Previous research has reported a lack of regular cancer screening among Chinese Americans. The overall objectives of this study were to use a mail survey of primary care physicians who served Chinese Americans in San Francisco to investigate: *a*) the attitudes, beliefs, and practices regarding breast, cervical, and colon cancer screening and *b*) factors influencing the use of these cancer screening tests. The sampling frame for our mail survey consisted of: *a*) primary care physicians affiliated with the Chinese Community Health Plan and *b*) primary care physicians with a Chinese surname listed in the Yellow Pages of the 1995 San Francisco Telephone Directory. A 5-minute, self-administered questionnaire was developed and mailed to 80 physicians, and 51 primary care physicians completed the survey. A majority reported performing regular clinical breast examinations (84%) and teaching their patients to do self-breast examinations (84%). However, the rate of performing Pap smears was only 61% and the rate of ordering annual mammograms for patients aged 50 and older was 63%. The rates of ordering annual fecal occult blood testing and sigmoidoscopy at regular intervals of three to five years among patients aged 50 and older were 69% and 20%, respectively. Barriers (patient-specific, provider-specific, and practice logistics) to using cancer screening tests were identified. The data presented in this study provide a basis for developing interventions to increase performance of regular cancer screening among primary care physicians serving Chinese Americans. Cancer screening rates may be improved by targeting the barriers to screening identified among these physicians. Strategies to help physicians overcome these barriers are discussed.

(Lee MM, Lee F, Stewart S, McPhee S. Cancer screening practices among primary care physicians serving Chinese Americans in San Francisco. West J Med 1999; 170:148–155)

Chinese Americans are a large and growing ethnic group in the United States. From 1980 to 1990, the Chinese population in the United States more than doubled to 1,645,472 people.[1] Data from the Surveillance Epidemiology and End Results (SEER) Program of the San Francisco Bay Area (1988–1992) showed that the five most common cancer sites among Chinese American men were lung, colorectal, prostate, liver, and oral cancer, and the five most common cancer sites among Chinese American women were breast, colorectal, lung, uterine, and ovarian cancer.[2] Early detection of many of these cancers, when treatment is more likely to be successful, can dramatically improve survival rates. Regular use of screening tests can detect cancers of the breast, colon, rectum, and cervix at an early stage. However, few data are available on cancer screening practices among Chinese Americans. Underutilization of cancer screening tests among Chinese Americans has been reported in a few previously published studies.[3–5] The Centers for Disease Control and Prevention's (CDC) Behavioral Risk Factor Surveillance System (BRFSS) conducted a survey on Chinese in Oakland during 1989–1990 showing that among Chinese women aged 40 and older, 68% reported never having a mammogram and 75% reported never having had a clinical breast examination.[4] In a recent telephone survey of Chinese women in San Francisco, California, the rates of having a mammogram (women aged 40 and older) and a Pap smear at regular intervals were 25% and 37%, respectively.[5] The low screening rates may be explained not only by patient characteristics and patient barriers to screening, but also by physician practice patterns.

Primary care physicians have the opportunity and ability to promote cancer screening practices among their

From the Department of Epidemiology and Biostatistics, University of California, San Francisco, California (Dr Lee and Ms Lee); Northern California Cancer Center, Union City, California (Dr Stewart); and Department of Medicine, University of California, San Francisco, California (Dr McPhee).

Reprint requests to Dr Marion Lee, Box 0560, University of California, San Francisco, CA 94143-0560 (e-mail: mlee@epi.ucsf.edu).

patients. Physicians increasingly function as gatekeepers to and coordinators of cancer prevention activities. Cancer screening tests such as mammography require a physician referral. The most often cited reason for not having a cancer screening test by patients, regardless of ethnicity, is that their physician has never recommended it.[6,7] Physician endorsement of a cancer screening test can have a positive impact on patient motivation.[8] Patients are more likely to have the screening test if they perceive that their physician strongly recommends the test.[9] Since Chinese greatly respect authority, the advice of physicians about cancer screening tests could be very effective in this ethnic population.

Despite the acceptance of a preventive philosophy among physicians and the establishment of cancer screening guidelines by national organizations,[10–16] many studies have documented a gap between recommended guidelines and physicians' screening practices.[15–19] Barriers to the practice of cancer screening among primary care physicians have been investigated.[18–26] These barriers include: *a*) lack of education, knowledge, and training (sigmoidoscopy, Pap smear); *b*) patient refusal (rectal exam, sigmoidoscopy, mammography, and Pap smear); *c*) patient discomfort or embarrassment (Pap smear, mammography and sigmoidoscopy); *d*) cost to patient (mammography and sigmoidoscopy); *e*) physician forgetfulness (clinical breast exam, mammography, fecal occult blood test); *f*) professional ambiguity and confusion of guidelines; and *g*) practice logistical difficulties, such as time constraints, availability of technology, personnel and office space. Those studies, however, did not specifically focus on physicians who serve predominantly Chinese American populations. To date, there are no reports in the literature that describe the prevalence of and barriers to prescribing cancer screening tests among physicians serving this ethnic population.

Recognizing the importance of studying the factors influencing cancer screening practices among patients and among their physicians, we focused on two converging pathways—the medical care system of providers (primary care physicians) and the sociocultural system of consumers (Chinese American women) in San Francisco. We studied interacting factors that influence practices of providers who prescribe the cancer screening tests and the actions of consumers in using these tests. A total of 775 Chinese American women completed a telephone survey. Results of the consumer survey have been previously published.[5] This paper describes the results of the physician mail survey.

In the physician mail survey, we examined screening practices regarding breast, cervical, and colorectal cancer among primary care physicians who served in San Francisco's Chinese community. The survey objectives were to assess the physicians': *a*) demographic and acculturation characteristics; *b*) practice settings; *c*) attitudes, beliefs, and practices (ie, compliance with specific cancer screening guidelines and screening intervals); *d*) perceived barriers and benefits of screening; and *e*) use of educational materials and follow-up/reminder systems relating to prescribing cancer-screening tests (clinical breast exam, mammogram, teaching breast self-exam, Pap smear, digital rectal exam, fecal occult stool test, and flexible sigmoidoscopy).

Methods

The sampling frame for our physician survey consisted of two samples of physicians: *a*) all primary care physicians who were affiliated with the Chinese Community Health Plan (CCHP) and *b*) all primary care physicians with Chinese surnames who were listed in the 1995 Yellow Pages of the San Francisco telephone directory. To be eligible, physicians were required to: *a*) have predominantly Chinese patients in their current practice in San Francisco and *b*) specialize in obstetrics and gynecology, internal medicine, family practice, or general practice. A 5-minute, self-administered questionnaire was developed to address our objectives. An invitation letter explaining the aims of the study along with a copy of the questionnaire and a stamped return envelope were sent to each eligible physician. Physicians who had not returned questionnaires after two weeks received a telephone call emphasizing the importance of the study and requesting their cooperation. A total of three phone calls were made to nonresponding physicians. Questionnaire data were then assessed for completeness and summarized. We determined the percentages of survey question responses. Standard statistical tests including chi-square statistics and student *t* tests were performed when appropriate.

Results

The survey was conducted during the spring of 1995. Of the 95 physicians (22 from the CCHP, 73 from the yellow pages), 80 physicians were found to be eligible, and 51 (68% from CCHP, 32% from yellow pages) completed the mail survey yielding a response rate of 62%.

The demographic characteristics and practice setting of the physicians are shown in Table 1. Most of the study physicians (84%) were male with a mean age of 50.2 years. About half of them (55%) were born in the United States. The majority (76%), however, obtained their medical degree in the United States. Half (48%) were internists and a quarter (24%) were family practitioners. About three-quarters of the physicians (77%) had an individual private practice. Their average length of time practicing in San Francisco was 13 years. Over half (62%) of their patients were Chinese. Most of their patients (61%) had either Medicaid or Medicare insurance. A majority of physicians (79%) and their staff (82%) were able to speak the Chinese language to their patients.

Table 2 shows breast and cervical cancer screening practices of primary care physicians. Although all physicians reported having ordered mammograms for their asymptomatic female patients, only 63% ordered annual mammograms for their patients aged 50 and older. Most

TABLE 1.—*Characteristics of Study Physicians and Their Practices (n = 51)*

	n	%
Demographic		
Male	43	84
Mean age (years) 50.2		
U.S. born	28	55
U.S. medical degree	38	76
Specialty		
Internal medicine	24	48
Family practice	12	24
Obstetrics/Gynecology	8	16
General practice	4	8
Other	2	4
Practice Setting		
Individual practice	39	77
Group practice	10	20
Ability to speak Chinese with patients		
Physician speaks Chinese	40	79
Staff speaks Chinese	42	82
Patient Characteristics		
Patients who are Chinese		62
Insurance status		
No insurance		12
Medicaid/Medicare		61

(84%) reported performing regular clinical breast examinations, while only 61% performed Pap smears in their office. More than half of the physicians followed specific guidelines for breast (75%) and cervical (55%) cancer screening (Table 3). The breast and cervical cancer screening guidelines of the American Cancer Society were the most frequently cited guidelines followed by the physicians.

For colorectal cancer screening (Table 4) fecal occult blood testing (FOBT) was most frequently recommended by study physicians: Sixty-nine percent reported ordering this test annually for asymptomatic patients aged 50 and older. About half (51%) of the physicians did not order regular sigmoidoscopy for patients older than age 50. One quarter (23%) of the physicians reported referring their patients to other physicians for this procedure. Only 20% of physicians performed sigmoidoscopy for patients aged 50 and older at regular intervals of three to five years. About half of the physicians did not follow any guidelines for colorectal cancer screening (Table 3). The colorectal cancer screening guidelines of the American Cancer Society

TABLE 2.—*Breast and Cervical Cancer Screening Practices Reported by Physician (n = 51)*

	n	%
Order mammograms	51	100
Interval for ordering mammograms for women older than 50		
Annually	32	63
Every two years	14	28
Perform regular clinical breast examinations	43	84
Teach patients to do breast self-examinations	43	84
Do Pap smears in office	31	61
Have cancer screening educational materials in Chinese	28	55

TABLE 3.—*Specific Guidelines Study Physicians Reported Following for Cancer Screening*

	Breast Cancer	Cervical Cancer	Colorectal Cancer
Follow no guidelines	13/51 (25%)	23/51 (45%)	27/51 (55%)
	n = 38	n = 28	n = 24
Follow guidelines of			
American Cancer Society	25 (66%)	17 (61%)	16 (67%)
American College OB/GYN	7 (18%)	8 (29%)	2 (8%)
National Cancer Institute	2 (5%)	0 (0%)	0 (0%)
Other	4 (10%)	3 (11%)	5 (25%)

TABLE 4.—*Colorectal Cancer Screening Practices Reported by Study Physicians (n = 51)*

	n	%*
Test recommended for colorectal cancer screening		
Digital rectal exam	13	25
Fecal occult blood testing	43	84
Sigmoidoscopy	10	20
Usual interval for ordering fecal occult blood testing for asymptomatic patients aged older than 50		
Annually	35	69
Every 2 years	8	16
Every 3 years	2	4
No usual interval	2	4
Do not order regular FOBT	2	5
Usual interval for ordering sigmoidoscopy for patients aged older than 50		
Annually	0	0
Every 2 years	2	4
Every 3–5 years	10	20
No usual interval	1	2
Do not order regular sigmoidoscopy	26	51
Refer to other physicians	12	23

*Percentage does not add up to 100% because some physicians declined to answer the question.

TABLE 5.—*Top Three Reasons for Not Prescribing Cancer Screening Tests Among Study Physicians (n = 51)*

Mammogram
1. Cost to patient (30%)
2. Patient concerned about pain or discomfort (28%)
3. Patient is healthy, has no physical symptoms, therefore, thinks tests unnecessary (26%)

Pap smear
1. Patient feels embarrassed, uncomfortable to have anyone exam her genitalia (29%)
2. Patient is healthy, has no physical symptoms, therefore thinks test unnecessary (29%)
3. Patient does not have the time, thinks test inconvenient (20%)

Fecal occult blood testing
1. Patient does not have the time, thinks test inconvenient (26%)
2. Cost to patient (13%)
3. Patient is healthy, has no physical symptoms, therefore thinks test unnecessary (9%)

Sigmoidoscopy
1. Patient concerned about pain or discomfort (58%)
2. Patient is healthy, has no physical symptoms, therefore thinks test unnecessary (33%)
3. Patient does not have the time, thinks test inconvenient (17%)

were the most frequently cited guidelines followed by the physicians.

Table 5 shows the three most frequently cited reasons by physicians for not prescribing the screening tests. "Patient feels healthy, has no physical symptoms; therefore, they feel the screening test is unnecessary" was a common reason cited by the physicians for not doing a Pap smear, ordering a mammogram, a fecal occult blood test, or a sigmoidoscopy. The primary barrier reported for not ordering a mammogram, however, was cost to the patient, and patient discomfort was the primary barrier for not ordering a sigmoidoscopy test. "Patient embarrassment," and "inconvenience to patient" were cited as the primary reasons for not ordering a Pap smear and fecal occult blood testing, respectively. The barriers reported by physicians for not performing clinical breast examinations were: *a*) inadequate training to perform clinical breast exam and *b*) feeling it was inappropriate to perform clinical breast examination when the patient came for other health problems.

The establishment of an effective reminder system can improve cancer prevention services in a medical practice.[27] Less than half of the study physicians, however, reported having a reminder system for clinical breast examination (38%), mammography (49%), digital rectal examination (35%), fecal occult blood test (41%), and sigmoidoscopy (21%).

Table 6 shows the attitudes towards breast cancer screening among study physicians. Seventy-six percent disagreed [somewhat (31%) + strongly (45%)] that screening mammograms were not cost effective for women. Seventy-three percent agreed [somewhat (53%) + strongly (20%)] that there was a general consensus regarding guidelines on breast cancer screening, and, 66% indicated that women should be allowed to refer themselves for breast cancer screening.

Table 7 presents the cancer screening practices by physician's age and specialty. Younger physicians performed more screening tests than older physicians. As expected, obstetrics/gynecology doctors performed more breast and cervical screening tests than other specialists. In particular, the differences in the percentage of physicians in each specialty performing Pap smears in asymptomatic women reached statistical significance.

Discussion

A majority of primary care physicians (84%) serving Chinese Americans in San Francisco reported performing regular clinical breast examinations and teaching breast self-examinations. The rate of performing Pap smears, however, was only 61%, and the rate of ordering annual mammograms for patients aged 50 and older was only 63%. The rates of ordering annual fecal occult blood testing and sigmoidoscopy at regular intervals of three to five years among patients aged 50 and older were 69% and 20%, respectively. This utilization rate is lower than published cancer screening guidelines and recommendations.[10–13]

One explanation for this low utilization rate could be that the physicians have no preference for any specific cancer screening guideline. Although a majority of physicians (75%) reported following specific guidelines for breast screening, only about half reported following specific guidelines for cervical (55%) and colorectal (47%) cancer screening. The cancer screening guidelines issued by the American Cancer Society were most

TABLE 6.—*Attitudes Toward Breast Cancer Screening Among Study Physicians (n = 51)**

	Strongly Agree	*Somewhat Agree*	*Somewhat Disagree*	*Strongly Disagree*
Screening mammograms are not cost-effective for women	3 (6%)	8 (16%)	16 (31%)	23 (45%)
There is a general consensus regarding guidelines on breast cancer screening	10 (20%)	27 (53%)	9 (18%)	5 (10%)
Women should be allowed to refer themselves for screening	17 (33%)	17 (33%)	12 (24%)	5 (10%)

*Frequencies may not add up to 100% because some did not answer the question.

TABLE 7.—*Self-Reported Cancer Screening Practices by Physician Age and Specialty*

	Age		Specialty		
	35–49 Years n = 28	*50–79 Years n = 22*	*Internal Med n = 24*	*Family & General Practice n = 18*	*OB/GYN n = 8*
Ordering annual screening mammograms for women aged 50+	21 (75%)	11 (50%)	12 (50%)	13 (72%)	7 (88%)
Performing regular, clinical breast exam	26 (93)	17 (77)	20 (83)	15 (83)	8 (100)
Doing Pap smears in asymptomatic women	20 (71)	11 (50)	11 (48)	12 (75)	8 (100)*
Recommending colorectal cancer screening					
Digital rectal exam	8 (29)	5 (23)	7 (29)	5 (28)	1 (13)
Fecal occult blood test	24 (86)	18 (86)	21 (88)	16 (89)	5 (63)
Sigmoidoscopy	7 (25)	3 (14)	6 (25)	2 (11)	2 (25)
Ordering annual fecal occult blood test	21 (75)	13 (59)	16 (67)	12 (67)	6 (75)
Interval for ordering sigmoidoscopy					
1–2 years	2 (7)	0 (0)	0 (0)	2 (11)	0 (0)
3–5 years	6 (21)	4 (18)	5 (21)	4 (22)	1 (13)

*$P = 0.05$

frequently cited. Confusion regarding the protocol and lack of agreement with the cancer screening recommendations issued by various organizations have been reported as reasons for not prescribing cancer screening tests by other physicians.[21,24] Seventy percent of physicians in our study stated that a general consensus exists regarding breast-cancer screening guidelines. At the time this survey was conducted, however, the mammography-screening guidelines among women aged 40 to 49 were controversial—for example, at that time the National Cancer Institute did not support regular mammographic screening for women aged 40 to 49 years old.[28] The extent to which physicians in our survey were knowledgeable about the content of guidelines that they claimed to follow was questionable. Our intention, however, was not to assess their knowledge or their adherence to specific cancer screening guidelines in this study.

Our study physicians reported lower levels of performance of six cancer screening tests [clinical breast exam (CBE), mammogram, Pap test, digital rectal exam, FOBT, and sigmoidoscopy] compared to those found in other national[15] and community[18–20,29] physician surveys. Prior studies have shown that physician self-reports often yield higher performance estimates for preventive services than patient reports or chart audits.[16,30,31] Since this study relies on self-reported data, it is possible that our physicians overreported their screening practices. Overreporting may be due to double-counting patients when the primary care physicians referred patients for screening tests to gynecology specialist who were also surveyed. Additionally, it is conceivable that those physicians who did not participate in our study were less likely to perform cancer screening examinations, thus further widening the gap between the performance rates in this population of physicians compared to rates reported in other physician surveys.

In our 1994 consumer telephone survey, only 31% of Chinese American women in the 50 to 74 age-group reported having a mammogram at regular intervals (>3 mammograms in the past 3 years).[5] Among Chinese American women aged 20 to 74 years old, 47% reported having a clinical breast examination (>2 CBEs within 3 years) and 37% reported having a Pap smear (>3 Pap smears in the past 5 years) at regular intervals.[5] However, in this 1995 physician survey of the same community, 63% of the study physicians reported ordering annual mammograms for patients age 50 and older, 84% reported performing regular CBEs and 61% reported performing Pap smears in the office. The discrepancy between screening rates reported by consumers and their physicians requires further investigation of the validity of such self-reported data.

Younger physicians (35–49 years old) in our study were more likely (although not statistically significant due to small sample size) to report prescribing cancer screening tests (mammogram, CBE, Pap smear, digital rectal exam, FOBT, and sigmoidoscopy) than older physicians (>50 years old). Older physicians may be more likely to subscribe to the traditional idea that because the patient feels healthy and has no physical symptoms, prescribing the screening tests is not necessary. Similarly, we found that older Chinese women who had not had Pap smears felt the test to be unnecessary at their age, particularly since no physical signs of any abnormalities were present.[5] The disinclination on the part of the patient as well as the physician make it even less likely that the test will be performed. These results point to a particular need to target older physicians' continuing education efforts regarding cancer screening tests.

Previous studies have shown that the prevalence of cancer screening activities varies by physician specialty.[32,17] Differences in prescribing screening tests in our physician survey were not demonstrated among different specialties except in performing Pap smears in asymptomatic women. Internists (48%) were significantly less likely than other specialty physicians [family

or general practitioners (75%) and gynecologists (100%)] to perform Pap smears. These differences may be due to age, type II errors, or too small a sample to find significant differences. Physician gender has also been shown to affect screening services.[33–35] A recent study has shown that patients of female, family, or general practitioners were more likely to receive Pap smears and mammograms than patients of male practitioners.[34] Since most of our respondents (84%) were men, we did not investigate for a physician gender effect.

The respondents to this study represented primary care physicians who served the Chinese population in San Francisco. Half of the physicians surveyed were drawn from a listing of Chinese surnames in the telephone directory Yellow Pages. Clearly, we might have excluded some non-Chinese physicians who served Chinese patients. In order to assess the representativeness of our participating physicians, we investigated the specialty of the 21 physicians who refused to participate in this study. We found the distribution to be similar to the participating physicians (57% internal medicine, 19% family practice, 14% OB/GYN, and 10% general practice).

The underuse of cancer screening tests by our study physicians might also be due to the physicians' difficulties in overcoming the barriers to cancer screening. Barriers to screening implementation were investigated in this study. They were divided into three categories: *a*) patient-specific barriers, *b*) provider-specific barriers, and *c*) practice logistical barriers. The most frequently cited patient-specific barriers to cancer screening were: *a*) cost (mammography, FOBT), *b*) pain or discomfort (mammography, sigmoidoscopy), *c*) patient reluctance, patient is healthy, patient feels test is unnecessary (mammography, Pap smear, FOBT, and sigmoidoscopy), *d*) embarrassment (Pap smear), and *e*) inconvenience or bother (Pap smear, FOBT, and sigmoidoscopy). The physician-specific barriers were: *a*) inadequate training for screening procedures, such as CBE, Pap smear, and sigmoidoscopy and *b*) physician discomfort with performing screening tests when the patient came for an unrelated problem (eg, performing CBE). The practice logistical barriers were: *a*) unavailability of reminder system for cancer screening and *b*) unavailability of educational materials in Chinese language.

Based on the above-reported barriers to cancer screening, we suggest the following strategies to increase the performance of regular cancer screening among primary care physicians. First, cost is always a concern for most patients. In our consumer survey, insurance status was associated with screening practices.[5] Chinese women with HMO and private health plans report higher screening tests than those not covered by insurance plans. In this study, 61% of patients were covered by either Medicaid or Medicare health insurance. As of January 1, 1998, Medicare beneficiaries now receive expanded coverage for breast, cervical, and colorectal cancer screening tests.[36] No deductible is required for annual mammograms for women aged 40 and older. Pap smears are covered every three years for average-risk women and annually for high-risk women. For the first time, coverage for regular colorectal cancer screening for asymptomatic Medicare patients is provided. Despite available insurance coverage, however, this population's lack of knowledge about the availability of such services as well as the extent of cost coverage acts as an additional economic barrier to screening. This lack of knowledge could be due largely to a language barrier. Physicians and their staffs can help their patients reduce their health costs by maximizing third-party payments and informing them about the expanded Medicare coverage. In addition, lack of knowledge about cost, availability of services, and extent of health insurance coverage may deter patients from seeking services. Thus, educational materials written in Chinese, which detail the resources of cancer screening, are necessary.

Second, although only a very small portion of patients experience significant discomfort in having screening examinations such as mammography,[37] physicians or technicians can explain to their patients the screening procedures and the expected discomfort experienced by some individuals. In counseling their patients, physicians need to address individual patient concerns and show their strong convictions regarding cancer screening tests. Performing regular cancer screening may be difficult for some physicians servicing Chinese patients, however, because many of these patients do not schedule regular appointments, but a large number of patients are seen each day for acute care on a drop-in basis. Referrals or recommendations for mammography could still be incorporated in this kind of practice setting.

Third, patient inconvenience contributes an obstacle to implementing fecal occult blood tests. Although explaining how to correctly do this test is time consuming for physicians, nurses or staff can be trained to emphasize the importance of performing the test correctly, and to educate patients in performing the test correctly. Physicians in this study perceived patient reluctance in taking the tests because the patients were healthy and felt the testing unnecessary. Chinese American women cited this same reason in the consumer telephone survey to explain why they did not have a mammogram and a Pap smear.[5] This finding suggests that patients need to be educated about the screening guidelines and the importance and benefits of regular cancer screening among healthy people.

Educational interventions targeted at physicians should emphasize the importance of educating patients through individual counseling and educational materials. Communicating with patients in their native language is most effective, especially since most of these patients are foreign-born. In our consumer survey, the ability to speak English was significantly associated with breast and cervical screening knowledge and practices.[5] A majority of study physicians and their staff could speak Chinese to their patients, and more than half had cancer screening educational materials (leaflets and

brochures) in Chinese language available in their offices. Development of culturally appropriate educational materials (eg, posters, pamphlets, brochures, and videotapes) in Chinese language is needed for Chinese-speaking patients.

Fourth, to alleviate patient-barrier factors such as embarrassment, educational interventions for physicians designed to improve communication skills are also necessary. Physicians need to be sensitive about the cultural issues that pervade this population. Male physicians may be less aware of the issues of personal modesty among Chinese women. An additional gender issue is that many women may be reluctant to undergo a breast or pelvic exam performed by a male physician. Modesty, respect for authority, degree of acculturation, and preconceptions about health and illness are factors that need to be addressed to encourage better screening use among Chinese men and women.

A lack of expertise or inadequate skills to perform particular screening procedures is sometimes a major physician-specific obstacle to performing screening tests. Technical skills training programs for physicians can improve the performance of clinical breast examinations and other screening procedures. Physicians learn proper techniques for performing clinical breast examinations in a training session. Some of our physicians reported that they would be uncomfortable in performing a clinical breast examination during a patient visit for an unrelated health problem. These physicians could handle the patient's immediate health problem and address patient concerns during that visit, but also set up an additional visit devoted to cancer screening. Since screening usually takes place during general check-up visits, the performance of cancer screening could be increased if such visits were systematically scheduled and if systems to remind physicians when and what screening tests were due (nurse-initiated flow chart, personal computer reminders, or chart-based reminders) were implemented. The effectiveness of reminder systems for physicians and their patients has been demonstrated in university and community practice settings.[27,38–42] Less than half of our study physicians, however, reported having a reminder system for cancer screening. Physicians and their staffs can set up an office reminder system (such as medical record checklist and flow sheets, stickers and alerts, or computer-generated reminders) directed at themselves, and a patient-directed reminder system (such as reminder postcards, letters, or telephone calls) to promote regular cancer screening.

To improve regular cancer screening among Chinese Americans, we need to explore further the pathway of the medical care system and to examine the interaction process between the providers (primary care physicians) and the consumers (Chinese Americans). Multiple logistic regression will be performed in the future to investigate the factors predicting screening practices among the consumers and their providers so that specific interventions to increase the use of regular screening can be developed.

Conclusions

This is the first study of breast, cervical, and colorectal cancer screening practices among primary care physicians serving Chinese Americans in San Francisco. Cancer screening rates can be improved by targeting barriers related to prescribing cancer screening tests by physicians. Strategies to help physicians overcome patient-specific barriers (patient refusal, cost to patient, inconvenience to patient, lack of knowledge), physician-specific barriers (lack of expertise or training in performing screening tests), and office system-specific barriers (lack of reminder system and educational materials in Chinese language) were suggested. The data presented in this study provided a basis for developing interventions to increase performance of regular, cancer screening among primary care physicians serving this important population.

Acknowledgment

This work was supported by the National Cancer Institute, Grant No. 5P01 CA55112.

REFERENCES

1. Asian and Pacific Islander Center for Census Information and Services. Our ten years of growth: a demographic analysis on Asian and Pacific Islander Americans. ACCIS Newsbrief; Fall 1922/Winter 1993:3

2. Perkins CI, Wright WE, Schlag R. Cancer incidence and mortality in California by race/ethnicity, 1988–1994. Sacramento, Calif, California Department of Health Services, Cancer Surveillance Section, 1997

3. Lew R, Thai V, Chen A. The health is wealth program: health promotion in the Oakland chinatown. Paper presented at: The Fifth Conference on Health Problems Related to the Chinese in North America, Toronto, 1990

4. Chen A, Lew R, Thai V, et al. Behavioral risk factor survey of Chinese in California 1989. Morbid Mortal Wkly Rep 1992; 41:266–269

5. Lee M, Lee F, Stewart S. Pathways to early breast and cervical cancer detection for Chinese American women. Health Educ Q 1996; 23(suppl):S76–S88

6. National Cancer Institute Breast Cancer Consortium. Screening mammography: a missed clinical opportunity? The results of the NCI Breast Screening Consortium and National Health Interview Studies. JAMA 1990; 264:54–58

7. National Health Interview Survey. Provisional estimates from the National Health Interview Survey: supplement on cancer control—United States, 1987. Morbid Mortal Wkly Rep 1988; 37:418–419

8. Burack RC, Liang J. The early detection of cancer in the primary-care setting: factors associated with the acceptance and completion of the recommended procedures. Prev Med 1987; 16:739–751

9. Rimer BK, Davis SW, Engstrom PF, Myers RE, Rosan JR. Some reasons for compliance and non-compliance in a health maintenance organization breast screening program. J Compliance Health Care 1988; 3:103–114

10. Leith AM, Dodd GD, Costanza M, et al. American Cancer Society guidelines for the early detection of breast cancer update 1997. CA Cancer J Clin 1997; 47:150–153

11. Byers T, Levin B, Rothenberger D, Dodd GD. American Cancer Society guidelines for screening and surveillance for early detection of colorectal polyps and cancer: update 1997. CA Cancer J Clin 1997; 47:154–160

12. American Cancer Society. Guidelines for the Cancer Related Checkup. Atlanta, GA, American Cancer Society; 1993

13. National Cancer Institute. Working Guidelines For Early Cancer Detection: Rationale and Supporting Evidence to Decrease Mortality. Bethesda, MD, National Cancer Institute, 1987

14. U.S. Preventive Services Task Force. Guide to Clinical Preventive Services: Report of the U.S. Preventive Services Task Force. 2nd ed. Baltimore, MD, Williams & Wilkins, 1996

15. 1989 survey of physicians' attitudes and practices in early cancer detection. CA Cancer J Clin 1990; 40:77–101

16. McPhee SJ, Richard RJ, Solkowitz SN. Performance of cancer screening in a university internal medicine practice: comparison with the 1980 American Cancer Society guidelines. J Gen Intern Med 1986; 1:275–281

17. Czaja R, McFall SL, Warnecke RB, Ford L, Kaluzny AD. Preferences of community physicians for cancer screening guidelines. Ann Intern Med 1994; 120:602–608

18. Gemson DH, Elinson J. Cancer screening and prevention: knowledge, attitudes, and practices of New York City physicians. NY State J Med 1987; 87:643–645

19. Costanza ME, Stoddard AM, Zapka JG, Gaw VP, Barth R. Physician compliance with mammography guidelines: barriers and enchancers. J Am Board Fam Pract 1992; 5:143–152

20. Rimer BK, Trock, Balshem A, Engstrom P, Rosan J, Lerman C. Breast screening practices among primary care physicians: reality and potential. J Am Bd Fam Pract 1990; 3:26–34

21. Williams P, Williams M. Barriers and incentives for primary care physicians in cancer prevention and detection. Cancer 1988; 61:2382–2390

22. Weinberger M, Saunders AF, Bearon LB, et al. Physician-related barriers to breast cancer screening in older women. J Gerontol 1992; 47(special issue):111–117

23. Resnicow KA, Schorow M, Bloom HG, Massad R. Obstacles to family practitioners' use of screening tests: determinants of practice? Prev Med 1989; 18:101–112

24. Wender RC. Cancer screening and prevention in primary care. Cancer 1993; 72:1093–1099

25. Frame PS. Screening flexible sigmoidoscopy: is it worthwhile? An opposing view. J Family Prac. 1987; 25:604–607

26. Mayer W, Beardall RW. Translating science into practice: cancer prevention in primary care medicine. In Greenwald P, Kramer BS, Weed D (Eds) Cancer Prevention and Control. New York, Marcel Dekker, 1995:411–433

27. McPhee SJ, Bird AJ, Fordham D, Jenkins CNH. Promoting cancer prevention by primary care physicians: results of a randomized, controlled trial. JAMA 1991; 266:538–544

28. Smigel K. NCI's proposed new breast cancer screening guidelines. J Natl Cancer Inst 1993; 85:1627

29. Clasen CM, Vernon SW, Mullen PD, Jackson GL. A survey of physician beliefs and self-reported practices concerning screening for early detection of cancer. Soc Sci Med 1994; 39: 841–849

30. Montano DE, Phillips WR. Cancer screening by primary care physicians: a comparison of rates obtained from physician self-report, patient survey, and chart audit. Am J Public Health 1995; 85:795–800

31. Woo B, Woo B, Cook EF, Weisberg M, Goldman L. Screening procedures in the asymptomatic adult: comparison of physicians' recommendations, patient desires, published guidelines, and actual practice. JAMA 1985; 254:1480–1484

32. Mann LC, Hawes DR, Ghods M, Bednar EJ, Potchen EJ. Utilization of screening mammography: comparison of different physician specialties. Radiology 1987; 164:121–122

33. Kreuter MW, Strecher VJ, Harris R, Kobrin SC, Skinner CS. Are patients of women physician screened more aggressively? A prospective study of physician gender and screening. J Gen Intern Med 1995; 10:119–125

34. Lurie N, Margolis KL, McGovern PG, Mink PJ, Slater JS. Why do patients of female physicians have higher rates of breast and cervical screening? J Gen Intern Med 1997; 12:34–43

35. Cassard SD, Weisman CS, Plichta SB, Johnson TL. Physician gender and women's preventive services. J Women Health 1997; 6:199–207

36. Clinton: Medicare to improve cancer screening. San Francisco Examiner. December 28, 1997:A2

37. Jackson VP, Lex AM, Smith DJ. Patient discomfort during screen-film mammography. Radiology 1988; 168:421–423

38. McPhee SJ, Detmer WM. Office-based interventions to improve delivery of cancer prevention services by primary care physicians. Cancer 1993; 72:1100–1112

39. McPhee SJ, Bird AJ, Jenkins CNH, Fordham D. Promoting cancer screening: a randomized trial of three interventions. Arch Intern Med 1989; 149:1866–1872

40. Fordham D, McPhee SJ, Bird JA, Rodnick JE, Detmer WM. The cancer prevention reminder system. MD Comput 1990; 7:289–295

41. Austin SM, Balas EA, Mitchell JA, Ewigman BG. Effect of physician reminders on preventive care: meta-analysis of randomized clinical trials. Proc Annu Symp Comput Appl Med Care 1994; 121–124

42. Lantz PM, Stencil D, Lippert MT, Beversdof S, Jaros L, Remington PL. Breast and cervical cancer screening in a low income managed care sample: the efficacy of physician letters and phone calls. Am J Public Health 1995; 85:834–836

Articles

Prevalence and Correlates of Hepatitis C Virus Infection Among Inmates Entering the California Correctional System

JUAN D. RUIZ, MD, DrPH; FRED MOLITOR, PhD; RICHARD K. SUN, MD, MPH; JOHN MIKANDA, MD, MPH; MATTHEW FACER, MS; *Sacramento, California*; JOHN M. COLFORD JR., MD, PHD; *Berkeley, California*; GEORGE W. RUTHERFORD, MD; *San Francisco, California*; MICHAEL S. ASCHER, MD; *Sacramento, California*

To estimate the prevalence and predictors of hepatitis C virus (HCV) infection among inmates, a cross-sectional survey was conducted in 1994 among inmates entering six reception centers of the California Department of Corrections. Discarded serum samples were tested for antibodies to human immunodeficiency virus (HIV), HCV, hepatitis B core, and hepatitis B surface antigen (HBsAg). Of 4,513 inmates in this study, 87.0% were men and 13.0% were women. Among male inmates, 39.4% were anti-HCV-positive; by race/ethnicity, prevalences were highest among whites (49.1%). Among female inmates, 53.5% were anti-HCV-positive; the prevalence was highest among Latinas (69.7%). In addition, rates for HIV were 2.5% for men and 3.1% for women; and for HBsAg, 2.2% (men) and 1.2% (women). These data indicate that HCV infection is common among both men and women entering prison. The high seroprevalence of anti-HCV-positive inmates may reflect an increased prevalence of high-risk behaviors and should be of concern to the communities to which these inmates will be released.

(Ruiz JD, Molitor F, Sun RK, Mikanda J, Facer M, Colford JM Jr, Rutherford GW, Ascher MS. Prevalence and correlates of hepatitis C virus infection among inmates entering the California correctional system. West J Med 1999; 170:156–160)

Hepatitis C virus (HCV), which was isolated and characterized by molecular cloning,[1] is the infectious agent in the majority of non-A, non-B hepatitis in the United States. Most cases are not associated with blood transfusions.[2] The majority of people infected with HCV may become chronically ill, and 60% of these develop chronic liver disease.[3] HCV is also a contributing cause of hepatocellular carcinoma.[4] Worldwide, the prevalence of antibodies to HCV ranges between 0.2% and 1.7%.[5] In the United States, prevalence is 1.8%.[6] An estimated 3.9 million Americans have been infected with HCV.[6]

Epidemiologic and experimental studies indicate that HCV is transmitted by the parenteral route (eg, injection drug users who share needles and syringes, health care workers with occupational exposure to blood, hemodialysis patients, and recipients of blood or blood products).[7] The highest HCV rates reported in the United States are related to injection drug use.[8] HCV may also be transmitted by other percutaneous exposures such as tattooing,[9] sexual or household contact,[10,11] transplantation of organs,[12] intranasal cocaine use,[13] and ear piercing in men.[13] The precise source of HCV infection, however, remains undetermined in approximately 10% of cases.[14]

Incarcerated populations are at risk for HCV infection by injection drug use and tattooing.[8,9,15] In countries outside the United States, prevalence rates for HCV infection among inmates have ranged from 4.6% to 50%.[9,15–21] Only one study to date has examined HCV seroprevalence among a US inmate population: Thirty-eight percent of 266 male inmates entering the Maryland prison system in 1985 and 1986 were found to be anti-HCV-positive.[22]

The purpose of our study was twofold: (1) to estimate the prevalence of infection with hepatitis C virus among inmates entering the California correctional system and (2) to identify predictors of the risk for HCV infection among this population.

Methods

The study protocol was reviewed and approved by the State of California Health and Welfare Agency, Committee for the Protection of Human Subjects.

From the California Department of Health Services, Sacramento, California, Office of AIDS, HIV/AIDS Epidemiology Branch (Drs Ruiz, Sun, Mikanda, and Mr Facer), the Maternal and Child Health Branch (Dr Molitor), and the Viral and Rickettsial Disease Laboratory (Dr Ascher); the University of California at Berkeley, Berkeley, California (Dr Colford); and the University of California at San Francisco, San Francisco, California (Dr Rutherford).

Reprint requests to Dr Juan D. Ruiz, California Department of Health Services, Office of AIDS, HIV/AIDS Epidemiology Branch, 611 N. 7th Street, Sacramento, CA 95814.

The site of entry into the California correctional system is determined according to the county where the crime was committed and by the type of crime. The California Department of Corrections (CDOC) has 13 reception centers (10 centers for male prisoners and 3 centers for female prisoners) where inmates are processed for entrance into the system. In California, all incoming inmates to the prison system receive a physical examination shortly after arrival at a reception center. A blood sample is obtained during the physical examination and tested for syphilis serology. The selection of reception centers for this study was made by the CDOC in collaboration with the California Department of Health Services, Office of AIDS. Facility selection was based on the following criteria: *1*) breadth of representation of urban and rural areas, *2*) high volume of inmates, *3*) regional representation, and *4*) routine blood specimen collection from all inmates for purposes other than this study.

This study included 4 of 10 reception centers where adult males are processed and 2 of 3 reception centers where adult females are processed. The four male reception centers selected were: *1*) R.J. Donovan Correctional Facility in San Diego (San Diego County), *2*) North Kern State Prison in Delano (Kern County), *3*) San Quentin State Prison in San Quentin (Marin County), and *4*) Wasco Reception Center in Wasco (Kern County). The two female reception centers selected were: *1*) California Institution for Women in Frontera (San Bernardino County) and *2*) Central California Women's Facility in Chowchilla (Madera County).

The sample size of this study was determined by using the 1994 prison population census and human immunodeficiency virus (HIV) prevalence estimates from the 1988 seroprevalence study among prisoners entering California prisons.[23] Based on a 2-tailed test for proportions, an alpha level of 0.05, statistical power of 0.80, and an attrition rate of 10% to detect a prevalence of 5%, the resulting gender-specific sample size for this study was 4,350 males and 650 females. The proportion of the sample selected from each reception center was based on the relative proportion of inmates processed at the centers on a weekly basis. Considering the actual gender-specific sample size for this study (3,926 male inmates and 587 female inmates), the final power was calculated as 0.67. The population in this study consisted of all inmates who had blood drawn in association with physical examinations upon entrance to the six reception centers from August 15, 1994 through September 9, 1994 (male inmates), and from August 15, 1994 through October 7, 1994 (female inmates). The study period for women was extended for an additional four weeks because of the relatively low number of incoming female inmates.

To obtain the least biased seroprevalence estimate of HCV among incoming inmates, we conducted a cross-sectional unlinked survey. Anonymous blood specimens collected for other purposes were tested in a manner that prevented linking test results to identifiable individuals. Sera from incoming inmates were eligible for inclusion in the study if: *1*) the specimen was drawn for syphilis serology as part of the initial admission process to the correctional facility (whether in detention status, awaiting sentencing, or convicted) and *2*) the inmate had not been incarcerated in the same facility during the survey period. Sera were tested for presence of antibody to hepatitis C virus (anti-HCV), HIV, and seromarkers of hepatitis B virus after all personal identifiers were removed.

For each subject, the public health nurses at the selected reception centers completed a standardized data collection form (Correctional Facility Seroprevalence Survey) provided by the Centers for Disease Control and Prevention. This form was completed for all eligible inmates who had a blood test ordered, even if sera could not be obtained, to allow comparison of inmates who were not tested with those who were tested for anti-HCV. Essential data collected for each eligible specimen included: sex, age group, race/ethnicity, previous incarceration information, and risk behavior information (available in some correctional facilities).

All testing was performed at the State Viral and Rickettsial Disease Laboratory in Berkeley, California. Sera were tested for the detection of antibody to hepatitis C virus by the Hepatitis C Virus Encoded Antigen (Recombinant c100-3, HC-31, and HC-34) Abbott HCV enzyme-linked immunosorbent assay (EIA) version 2.0. Sera that were reactive on the initial EIA were reported as having antibody detected. Approximately 10% of reactive specimens were then confirmed by Hepatitis C Virus Encoded Antigen/Peptide (Recombinant c33c and NS5 antigens; Synthetic 5-1-1, c100, and c22 peptides), Chiron, RIBA, HCV 3.0 Strip Immunoblot Assay.

Statistical analyses were conducted using SAS-PC version 6.10 (Statistical Analysis System for Personal Computers, Cary, NC) and Epi Info version 6.0.[24] Frequency distributions were compared using chi-square tests for independent samples. Ninety-five percent confidence intervals (CIs) for prevalences of HCV were calculated assuming a binomial distribution for the numbers testing positive. When the number testing positive was less than five, Fisher's exact limits were calculated. Prevalences in subgroups were compared using ratios of rates as estimates of relative risk. Exact binomial 95% confidence intervals were calculated for odds ratios using Epi Info version 6.0. Seroprevalences were computed excluding missing/unknown values.

We performed stepwise logistic regressions using SAS 6.10 to identify significant factors for anti-HCV-positivity. We constructed each model using a P value of 0.05 (based on the maximum likelihood ratio method) as both the entry and removal criterion. We computed adjusted odds ratios (ORs) with corresponding 95% CIs for the different levels of the significant independent covariates in the logistic regression models.[25] The results of our analyses are presented for male and female inmates separately. All two-way interactions were included in the model building process. We limited our analyses to samples from white, African American, and Latina/o inmates.

Results

During the study period, 5,279 inmates received intake physical examinations at the six reception centers

selected for the study. Of these, 97.4% (n = 5,142) had serum tested for the presence of anti-HCV. Sera were not tested for the remaining inmates (n = 137) because no blood was drawn, the quantity of the sample was not sufficient, or the specimen was not saved. Results of this paper are based on 4,513 serum specimens for white, African American, and Latina/o inmates. The remaining specimens (n = 629) were coded as other race/ethnicity (n = 216) or unidentified race/ethnicity (n = 413).

Of the 4,513 inmates, 87% (n = 3,926) were male and 13% (n = 587) were female. Male and female inmates were predominantly between 25 and 39 years of age (61.9% and 69.5%, respectively). Among male inmates, 35.9% were Latino, 32.9% African American, and 31.2% white. Among female inmates, 38.7% were white, 36.6% African American, and 24.7% Latina.

Of the 3,926 male inmates, 1,545 (39.4%; 95% CI, 37.8–40.9) were anti-HCV-positive upon entry into prison as compared with 314 of 587 (53.5%; 95% CI, 49.4–57.6) female inmates. Among male inmates, 2.5% were HIV positive and 2.2% were HBsAg positive. Among female inmates, rates were 3.1% and 1.2% for HIV and HBsAg, respectively.

The prevalence of anti-HCV positivity was highest for both male and female inmates 25 years or older (46.2% and 55.4%, respectively) (Table 1). White males had a higher prevalence (49.1%) than African Americans or Latinos. In univariate analyses of male inmates, hepatitis C infection was associated with inmates aged 25 or older who had a prior incarceration history, were HIV-positive, were anti-hepatitis B core (HBc)–positive, and were hepatitis B surface antigen (HBsAg)–positive. In univariate analyses of female inmates, HCV infection was associated with inmates aged 25 or older who were of Latina ethnicity, had a prior incarceration history, were HIV-positive, and were anti-HBc-positive (Table 1).

Table 2 shows the results of multivariate analyses of factors associated with HCV infection among male and female inmates. Among male inmates, we found anti-HBc-positivity (OR = 10.64; 95% CI, 8.91–12.72), aged 25 or older (OR = 4.01; 95% CI, 3.09–5.21), and previous incarceration history (OR = 2.28; 95% CI, 1.92–2.70) to be independent risk factors for HCV seropositivity. To be of African American race (OR = 0.35; 95% CI, 0.29–0.41) had a significant protective effect. Among female inmates, the risk factors associated with HCV infection in a multivariate model were: HIV positivity (OR = 9.35; 95% CI, 1.80–48.73), anti-HBc positivity (OR = 8.10; 95% CI, 5.44–12.10), and Latina ethnicity (OR = 1.70; 95% CI, 1.02–2.81).

Table 3 includes the results of coinfection with other serological markers among anti-HCV-positive and anti-HCV-negative male and female inmates. Among anti-HCV-positive male inmates, 27.2% had no other serological markers, and 62.2% were anti-HBc positive as compared with 84.8% and 11.3%, respectively, among anti-HCV-negative male inmates. Among anti-HCV-positive female inmates, 21.7% had no other serological markers and 68.5% were anti-HBc positive as compared with 75.8% and 20.9%, respectively, among anti-HCV-negative female inmates.

TABLE 1.— *Subgroup-Specific Hepatitis C Virus (HCV) Seroprevalence Among Inmates Entering the California Correctional System, 1994**

	Number in sample		HCV Prevalence per 100 inmates (95% CI)		Odds Ratio (95% CI)	
Subgroup	Men	Women	Men	Women	Men	Women
Age group						
24 or younger	801	3,125	12.6 (10.4–15.1)	37.1 (25.2–50.3)	1.0	1.0
25 or older	62	525	46.2 (44.4–48.0)	55.4 (51.1–59.7)	5.96 (4.76–7.48)	2.14 (1.20–3.81)
Race/ethnicity						
White	1,223	226	49.1 (46.3–51.9)	58.1 (51.4–64.6)	1.0	1.0
African American	1,292	214	29.2 (26.7–31.7)	37.7 (31.2–44.5)	0.43 (0.36–0.50)	0.43 (0.29–0.70)
Latina/o	1,408	144	40.2 (37.6–42.8)	69.7 (61.5–77.0)	0.70 (0.60–0.82)	1.67 (1.05–2.67)
Previous incarceration						
No	1,659	245	27.0 (24.9–29.3)	47.6 (41.2–54.0)	1.0	1.0
Yes	2,088	332	49.0 (46.9–51.2)	58.6 (53.1–63.9)	2.60 (2.26–2.99)	1.56 (1.10–2.20)
HIV						
Negative	3,820	566	38.8 (37.3–40.4)	52.6 (48.4–56.7)	1.0	1.0
Positive	97	18	61.9 (51.4–71.5)	88.9 (65.3–98.6)	2.56 (1.66–3.95)	7.19 (1.57–12.1)
Anti-HBc						
Negative	2,692	312	21.7 (20.1–23.3)	31.7 (26.6–37.2)	1.0	1.0
Positive	1,231	272	78.0 (75.6–80.3)	78.6 (73.4–83.5)	12.9 (10.9–15.2)	8.1 (5.5–12.1)
HBsAg						
Negative	3,820	568	38.9 (37.3–40.5)	53.8 (49.6–57.9)	1.0	1.0
Positive	86	7	58.1 (47.0–68.7)	42.9 (9.9–81.6)	2.18 (1.39–3.44)	0.64 (0.11–3.42)

* Statistical analyses were conducted using SAS-PC version 6.10 and Epi Info version 6.0

TABLE 2.—*Multivariate Logistic Regression Analyses for Hepatitis C Virus (HCV) Seropositivity Among Male and Female Inmates Entering the California Correctional System, 1994**

Variable	Male Inmates OR (95% CI)	Female Inmates OR (95% CI)
Age group		
24 or younger	1.00	—
25 or older	4.01 (3.09–5.21)	—
Race		
Non-African American	1.00	—
African American	0.35 (0.29–0.41)	—
Non-Latina	—	1.00
Latina	—	1.70 (1.02–2.81)
Previous incarceration		
No	1.00	—
Yes	2.28 (1.92–2.70)	—
HIV		
Negative	—	1.00
Positive	—	9.35 (1.80–48.73)
Anti-HBc		
Negative	1.00	1.00
Positive	10.64 (8.91–12.72)	8.10 (5.44–12.10)

*Statistical analyses were conducted using SAS-PC version 6.10 and Epi Info version 6.0

Two hundred twelve anti-HCV reactive results were tested by a RIBA HCV 3.0 Strip Immunoblot confirmatory assay and over 90% (203) of the specimens were confirmed positive by this method.

Some correctional facilities collected risk behavior information as part of the admission process. If risk behavior data were obtained during the admission process, this information was matched for each specimen. Risk behavior information was provided for 831 (18.4%) of the 4,513 inmates. The most frequent risk behavior for HCV infection, reported in 805 (96.9%) of the 831 inmates, was injection drug use since 1978. Among the 549 male inmates who had used injection drugs since 1978, 430 (78.3%) were anti-HCV positive; among the 256 female inmates in this category, 181 (70.7%) were anti-HCV positive.

Discussion

In this study of inmates entering the California correctional system, we found that the overall prevalence of HCV infection was 41.2%, and the prevalence was higher in female inmates (53.5%) than male inmates (39.4%). This serosurvey provides public health officials with important information about HCV infection among California inmates.

Although we were able to collect risk behaviors in only 18% of the inmates, the high prevalence of HCV infection in both male and female inmates suggests that this population has engaged in high-risk behaviors. In this study, a vast majority of HCV-positive inmates reported injecting drugs since 1978. This risky behavior is also associated with transmission of other viruses such as HIV and HBV.

Our findings on HCV infection complement previous studies conducted among inmates in the United States and other parts of the world. Among male inmates in these studies, the prevalence of HCV infection has ranged from 28.0% to 49.8%.[15,16,18,19,21] In female inmates, the seroprevalence was 39.8%.[17] Some studies did not differentiate between male and female inmates.[8,15,20]

The high seroprevalence of HCV infection among inmates entering prison should be a serious concern to public health officials, health care providers, and policymakers for the following reasons: (1) infected male and female inmates may continue to engage in high-risk behaviors and infect others while in custody, (2) providing health care services for HCV-infected inmates with chronic liver disease or hepatocellular carcinoma is costly, and (3) infected inmates may transmit the disease to people in communities into which they are released.

Neither vaccine nor postexposure prophylaxis are available for HCV infection, and immunoglobulin is not recommended. The use of alpha interferon during the acute phase of hepatitis C may result in a decrease in the

TABLE 3.—*Markers for Co-infection with HIV and HBV Among Anti-HCV Positive and Anti-HCV-Negative Male and Female Inmates**

Seralogical Marker	Men		Women	
	Anti-HCV (+) (n = 1,545) n (%)	Anti-HCV (–) (n = 2,381) n (%)	Anti-HCV (+) (n = 314) n (%)	Anti-HCV (–) (n = 273) n (%)
No HIV or HBV markers	420 (27.2)	2,019 (84.8)	68 (21.7)	207 (75.8)
HIV(+)	60 (3.9)	37 (1.6)	16 (5.1)	2 (0.7)
Anti-HBc (+)	961 (62.2)	270 (11.3)	215 (68.5)	57 (20.9)
HBsAg (+)	50 (3.2)	36 (1.5)	3 (0.9)	4 (1.5)
Anti-HBc (+) and HIV (+)	47 (3.0)	17 (0.7)	12 (3.8)	1 (0.4)
HBsAg (+) and HIV (+)	4 (0.3)	2 (0.08)	0 (0.0)	1 (0.4)
Anti-HBc (+) and HBsAg (+) and HIV (+)	3 (0.2)	2 (0.08)	0 (0.0)	1 (0.4)

*Statistical analyses were conducted using SAS-PC version 6.10 and Epi Info version 6.0

rate of chronicity.[26] The currently recommended therapy for chronic hepatitis C is a 12- to 18-month course of alpha interferon in doses of 3 million units, three times a week; a regimen that results in sustained clearance of HCV RNA in approximately 20% of patients.[26] Recently, the Food and Drug Administration approved Rebetron Combination Therapy (Intron A [interferon alpha-2B recombinant for injection] and Rebetol [ribavirin] capsules) for use in hepatitis C patients who have not been treated with alpha interferon therapy.[27]

Primary prevention of HCV transmission depends on measures such as universal precautions in the occupational setting,[7] safer needle-using practices,[8] and routine HCV screening of blood and plasma donors and donors of organs, tissues, and semen.[7] Other primary prevention practices must include viral inactivation of plasma-derived products or the assurance that these products are HCV RNA negative by reverse transcription–polymerase chain reaction.[14] Inmate education and counseling are important in preventing HIV, HBV, and HCV infections. Counseling must be culturally appropriate and at a level of comprehension that is consistent with the learning skills of the inmate. An assessment of the risk-factor profile of all inmates entering the correctional system should be conducted. Prevention strategies designed to encourage voluntary behavior change and to facilitate effective risk-reduction counseling should be planned and implemented.

Interpretations of the results of this study are subject to limitations. We cannot be certain if the characteristics of inmates included in this study are generalizable to all inmates in the California correctional system. In 1994, the California Department of Corrections did not collect risk information from all inmates as they entered the system. Therefore, we had limited individual risk information data for determining modes of transmission of HCV. We were unable to examine inmates' past histories of sexually transmitted diseases and assess any association with HCV infection. Syphilis serology results were not available to us at the time survey data were collected. Much work remains to be done to complete our understanding of the dynamics of transmission and infection with HCV. At the state and local level, the highest priorities for epidemiologic research are to understand better the precise populations at risk of incident infections and to use this information to direct and monitor specific, prevention programs that are likely to be effective for at-risk populations. Further serosurveys and behavioral epidemiologic studies should be undertaken to monitor the seroprevalence and trends of prevalent infections in this population and to use this information to direct and monitor effectiveness of specific prevention programs for inmates.

Acknowledgments

The authors would like to thank Ms Cynthia Cossen and the staff from the Viral and Rickettsial Disease Laboratory in Berkeley; Dr Susann Steinberg, Mr Kevin May and the public health nurses from the California Department of Corrections; Mr Michael Hughes, MS, currently with the Department of Veterans Affairs, San Francisco, California; and the Prevention Services Research Branch, Centers for Disease Control and Prevention, Atlanta, Georgia

REFERENCES

1. Choo Q-L, Kuo G, Weiner AJ, Overby LR, Bradley DW, Houghton M. Isolation of a cDNA clone derived from a blood-borne non-A, non-B viral hepatitis genome. Science 1989; 244:349–362

2. Alter MJ, Hadler SC, Judson FN, et al. Risk factors for acute non-A, non-B hepatitis in the United States and association with hepatitis C virus infection. JAMA 1990; 264:2231–2235

3. Alter MJ, Margolis HS, Krawczynski K, et al. The natural history of community-acquired hepatitis C in the United States. N Engl J Med 1992; 327:1899–1905

4. Kiyosawa K, Sodeyama T, Tanaka E, et al. Interrelationship of blood transfusion, non-A, non-B hepatitis and hepatocellular carcinoma: analysis by detection of antibody to hepatitis C virus. Hepatology 1990; 12:671–675

5. Bradley DW. Virology, molecular biology, and serology of hepatitis C virus. Transfusion Med Rev 1992; VI:93–102

6. Alter MJ. Epidemiology of hepatitis C. Hepatology 1997; 26:62S–65S

7. Centers for Disease Control and Prevention. Public health service interagency guidelines for screening donors of blood, plasma, organs, tissues, and semen for evidence of hepatitis B and hepatitis C. Morb Mortal Wkly Rep 1991; 40(RR-4):1–13

8. Alter MJ, Mast EE. The epidemiology of viral hepatitis in the United States. Gastroenterol Clin N Am 1994; 23:437–455

9. Holsen DS, Harthug S, Myrmel H. Prevalence of antibodies to hepatitis C virus and association with intravenous drug abuse and tattooing in a national prison in Norway. Eur J Clin Microbiol Inf Dis 1993; 12:673–676

10. Alter MJ, Hadler SC, Judson FN, et al. Risk factors for acute non-A, non-B hepatitis in the United States and association with hepatitis C virus infection. JAMA 1990; 264:2231–2235

11. Stevens CE, Taylor PE, Pindyck J, et al. Epidemiology of hepatitis C virus. A preliminary study in volunteer blood donors. JAMA 1990; 263:49–53

12. Nowicki MJ, Ahmad N, Heubi JE, Kuramoto JK, Baroudy BM, Balistrevi WF. The prevalence of hepatitis C virus (HCV) in infants and children after liver transplantation. Dig Dis Sci 1994; 39:2250–2254

13. Conry-Cantilena C, VanRaden M, Gibble J, et al. Routes of infection, viremia, and liver disease in blood donors found to have hepatitis C virus infection. N Engl J Med 1996; 334:1691–1696

14. Centers for Disease Control and Prevention. Recommendations for prevention and control of hepatitis C virus (HCV) infection and HCV-related chronic disease. Morb Mortal Wkly Rep 1998; 47(RR-19):1–39

15. Crofts N, Stewart T, Hearne P, Ping XY, Breshkin AM, Locarnini SA. Spread of bloodborne viruses among Australian prison entrants. BMJ 1995; 310:285–288

16. Prefontaine RG, Chaudhary RK. Seroepidemiologic study of hepatitis B and C viruses in federal correctional institutions in British Columbia. Can Dis Wkly Rep 1990; 16–25:265–268

17. Ford PM, White C, Kaufmann H, et al. Voluntary anonymous linked study of the prevalence of HIV infection and hepatitis C among inmates in a Canadian federal penitentiary for women. Can Med Assoc J 1995; 153:1605–1609

18. Anand CM, Fonseca K, Walle RP, Powell S, Williams M. Antibody to hepatitis C virus in selected groups of a Canadian urban population. Int J Epidemiol 1992; 21:142–145

19. Anon C, DelOlmo JA, Llovet F, et al. The hepatitis C virus among the prison population of Valencia. Rev Esp Enferm Dig 1995; 87:505–508

20. Katayama Y, Barzaga NG, Alipio A, et al. Genotype analysis of hepatitis C virus among blood donors and inmates in Metro Manila, The Philippines. Microbiol Immunol 1996; 40:525–529

21. Utsumi T, Hashimoto E, Okumura Y, et al. Heterosexual activity as a risk factor for the transmission of hepatitis C virus. J Med Virol 1995; 46:122–125

22. Vlahov D, Nelson KE, Quinn TC, Kendig N. Prevalence and incidence of hepatitis C virus infection among male prison inmates in Maryland. Eur J Epidemiol 1993; 9:566–569

23. Singleton JA, Perkins CI, Trachtenberg AI, Hughes MJ, Kizer KW, Ascher M. HIV antibody seroprevalence among prisoners entering the California correctional system. West J Med 1990; 153:394–399

24. Dean AG, Dean JA, Coulombier D, et al. Epi Info Version 6.0: A Word Processing, Database, and Statistics Program for Epidemiology on Microcomputers. Atlanta, Georgia: Centers for Disease Control and Prevention; 1994

25. Hosmer DW, Lemeshow S. Applied Logistic Regression. New York, NY: John Wiley and Sons; 1989

26. Hoofnagle JH. Therapy of viral hepatitis. Digestion 1998; 59:563–578

27. Food and Drug Administration Web site. Available at: http://www.fda.gov/bbs/topics/ANSWERS/ANS00929.html.

Articles

Primary Mediastinal Malignancies: Findings in 219 Patients

ROY TEMES, MD; THERESA CHAVEZ, CTR; DOUGLAS MAPEL, MD; LOREN KETAI, MD; RICHARD CROWELL, MD; CHARLES KEY, MD; FABRIZIO FOLLIS, MD; STUART PETT, MD; JORGE WERNLY, MD; *Albuquerque, New Mexico*

The purpose of this study was to determine the demographics, histology, methods of treatment, and survival in primary mediastinal malignancies. We did a retrospective review of the statewide New Mexico Tumor Registry for all malignant tumors treated between January 1, 1973 and December 31, 1995. Benign tumors and cysts of the mediastinum were excluded. Two hundred nineteen patients were identified from a total of 110,284 patients with primary malignancies: 55% of tumors were lymphomas, 16% malignant germ cell tumors, 14% malignant thymomas, 5% sarcomas, 3% malignant neurogenic tumors, and 7% other tumors. There were significant differences in gender between histologies ($P < 0.001$). Ninety-four percent of germ cell tumors occurred in males, 66% of neurogenic tumors were in females; other tumors occurred in males in 58% of cases. There were also significant differences in ages by histology ($P < 0.001$). Neurogenic tumors were most common in the first decade, lymphomas and germ cell tumors in the second to fourth decades, and lymphomas and thymomas in patients in their fifth decades and beyond. Stage at presentation ($P = 0.001$) and treatment ($P < 0.001$) also differed significantly between histologic groups. Five-year survival was 54% for lymphomas, 51% for malignant germ cell tumors, 49% for malignant thymomas, 33% for sarcomas, 56% for neurogenic tumors, and 51% overall. These survival rates were not statistically different ($P > 0.50$). Lymphomas, malignant germ cell tumors, and thymomas were the most frequently encountered malignant primary mediastinal neoplasms in this contemporary series of patients. Demographics, stage at presentation, and treatment modality varied significantly by histology. Despite these differences, overall five-year survival was not statistically different.

(Temes R, Chavez T, Mapel D, Ketai L, Crowell R, Key C, Follis F, Pett S, Wernly J. Primary mediastinal malignancies: findings in 219 patients. West J Med 1999; 170:161–166)

Mediastinal malignancies are uncommon. Consequently, contemporary series using modern diagnostic and therapeutic modalities are rare. We reviewed the statewide New Mexico Tumor Registry for all cases of mediastinal malignancy diagnosed during the years 1973 through 1995.

Materials and Methods

The New Mexico Tumor Registry National Cancer Institute Surveillance, Epidemiology, and End Results program (SEER) statewide data base was used to abstract all cases of malignant, primary tumors diagnosed between January 1, 1973 and December 31, 1995 within the state of New Mexico. This registry contains all primary tumors diagnosed within the state and is not selected by treatment center, treatment type, physician, or referral pattern. From these cases, some were selected for further analysis using identifiers for primary sites of origin from thymus; anterior, posterior, or not otherwise specified mediastinum; intrathoracic lymph nodes; heart; peripheral nerves and autonomic nervous system of the thorax. Primary tumors of the thyroid, parathyroid, airway, esophagus, and lung were excluded. Statistical analysis was performed using Fisher exact test for binary variables, Wilcoxon rank sum test for non-normally distributed data, life table analysis for survival data, and Kruskal-Wallis analysis for age distributions.

Results

Two hundred nineteen patients with primary mediastinal malignancies were identified from a population of 110,284 patients with primary malignant tumors.

From the Department of Surgery (Drs Temes, Follis, Pett, and Wernly), Division of Thoracic and Cardiovascular Surgery; the New Mexico Tumor Registry (Ms Chavez and Dr Key); the Department of Medicine (Dr Crowell); and the Department of Radiology (Dr Ketai), University of New Mexico School of Medicine, Albuquerque, New Mexico. Work performed at the University of New Mexico School of Medicine.

Reprint requests to R. Thomas Temes, MD, University of New Mexico, Department of Surgery, 2211 Lomas Boulevard NE, Albuquerque, NM 87131 (e-mail: Ttemes@salud.unm.edu).

TABLE 1.—*Histologic Classification of Primary Mediastinal Malignancies*

Histalagy	No. Pts.	%
Lymphoproliferative	121	55
Hodgkin's	42	
Non-Hodgkin's	79	
Germ cell	34	16
Seminoma	17	
Nonseminoma	17	
Thymoma	31	14
Sarcoma	12	5
Neurogenic	6	3
Neuroblastoma	5	
Ganglioneuroblastoma	1	
Other	15	7
Total	219	100

TABLE 3.—*Treatment Modalities for Primary Mediastinal Malignancies**

Histalagy	Surgery (%)	MED (%)	XRT (%)	Na Treatment
Lymphoproliferative	16 (15)	85 (77)	58 (53)	11
Hodgkin's	6	27	29	1
Non-Hodgkin's	10	58	29	10
Germ cell	17 (50)	26 (76)	15 (44)	0
Seminoma	6	12	7	0
Nonseminoma	11	14	8	0
Thymoma	19 (63)	13 (43)	21 (70)	1
Sarcoma	8 (89)	6 (67)	5 (56)	3
Neurogenic	5 (100)	0 (0)	1 (20)	1
Other	8 (72)	2 (18)	10 (91)	4
Total	73 (37)	132 (66)	110 (55)	20

*Percentages are treated patients receiving modality as part or all of treatment.

Sixty-three percent were male (138/219) and 37% were female (81/219). Median age was 47 years. Sixty-eight percent (149/219) were non-Hispanic whites, 27% (60/219) were Hispanic whites, 3% (6/219) were Native American, and less than 2% were black or of other ethnicity. Histologic confirmation was present in 95% of patients (209/219).

Table 1 shows tumor histology. A total of 51 histologic subtypes were diagnosed. Lymphoproliferative malignancies were most common and present in 55% of patients. Other tumor classes, listed in decreasing order of frequency, were malignant germ cell tumor in 16% of patients, malignant thymoma in 14%, sarcoma in 5%, neurogenic malignancy in 3%, and other malignancies in 7%.

Table 2 presents staging. Localized disease, defined as a tumor confined entirely to the organ of origin, was present in 40% of patients; regional disease, defined as disease extending directly into surrounding organs or tissues and/or involving regional lymph nodes, was present in 27%; and distant disease, defined as tumor spread to remote areas of the body, was present in 29%. Staging was unknown in 5% of patients. In tumors other than lymphoma, staging was localized in 28% (27/98), regional in 38% (37/98), remote in 29% (28/98), and unknown in 6% (6/98).

Table 3 lists treatments. Medical therapy (MED) was used most commonly and was part or all of treatment in 66% of treated patients. Medical therapy consisted primarily of chemotherapy, but by definition within the registry, also included any hormonal or immunotherapy. Radiation therapy (XRT) was part or all of treatment in 55%, and surgery was part or all of treatment in 37% of the total group and in 63% (57/90) of treated patients without lymphoproliferative malignancies.

Table 4 lists survivals. Five-year survival was 51% for the entire group. Survival was 54% for lymphoma, 51% for malignant germ cell tumors, 49% for malignant thymoma, 33% for sarcoma, and 56% for neurogenic tumors.

Lymphoproliferative malignancies were subtyped as Hodgkin's lymphomas in 35% and non-Hodgkin's

TABLE 2.—*Staging of Primary Mediastinal Malignancies*

Histalagy	Local (%)	Region. (%)	Distant (%)	Unkn. (%)
Lymphoproliferative	60 (50)	22 (18)	35 (29)	4 (3)
Hodgkin's	20	7	14	1
Non-Hodgkin's	40	15	21	3
Germ cell	7 (21)	13 (38)	12 (35)	2 (6)
Seminoma	4	7	6	0
Nonseminoma	3	6	6	2
Thymoma	5 (16)	15 (48)	9 (29)	2 (7)
Sarcoma	7 (58)	1 (8)	4 (33)	0 (0)
Neurogenic	3 (50)	2 (33)	1 (17)	0 (0)
Other	5	6	2	2
Total	87 (40)	59 (27)	63 (29)	10 (5)

TABLE 4.—*Five-Year Survival Percentages by Histology of Primary Mediastinal Malignancies*

Histalagy	Localized	Regianal	Distant	Overall
Lymphoproliferative	55	64	43	54
Hodgkin's	85	78	62	77
Non-Hodgkin's	39	59	30	43
Germ cell	37	53	48	51
Seminoma	36	86	46	62
Nonseminoma	33	17	50	40
Thymoma	100	62	0	49
Sarcoma	57	0	0	33
Neurogenic	67	0	0	56
Total	57	55	35	51

lymphomas in 65% (Table 1). The most common lymphomas were nodular sclerosing Hodgkin's disease in 26% (32/121) and large-cell diffuse malignant lymphoma in 26% (32/121). Fifty-seven percent (69/121) of patients were male and 43% (52/121) female. There was no significant difference in gender distribution between Hodgkin's and non-Hodgkin's lymphomas (22/42 vs 47/79 males, $P > 0.5$). The median age was 45 (range 2–96) years for all lymphomas; the median age for Hodgkin's was significantly younger than the median age of non-Hodgkin's (28 Hodgkin's, range 11–71; 54 non-Hodgkin's, range 2–96; $P < 0.001$).

Lymphomas were staged as localized in 50% of patients, regional in 18%, remote in 29%, and unknown in 3% (Table 2). In treated patients, MED was part or all of treatment in 77% of patients (27/41 Hodgkin's, 58/69 non-Hodgkin's, $P = 0.04$); XRT was part or all of treatment in 53% of patients (29/41 Hodgkin's, 29/69 non-Hodgkin's, $P = 0.001$); and surgery was part or all of treatment in 15% of patients (6/41 Hodgkin's, 10/69 non-Hodgkin's, $P > 0.5$) (Table 3).

The five-year survival for patients with lymphoma was 54% (Table 4). Five-year survival for Hodgkin's disease was 77% and for non-Hodgkin's lymphoma was 43% ($P < 0.001$). Five-year survival of localized Hodgkin's disease was 85% compared to 39% for non-Hodgkin's lymphoma ($P = 0.001$).

Malignant germ cell tumors were subtyped as seminomas in 50% and nonseminomas in 50% (Table 1). The most common nonseminomatous tumor was malignant, mixed germ-cell tumor in 35% (6/17). Ninety-four percent of patients were male (17/17 seminoma, 15/17 nonseminoma, $P > 0.5$). Median age for the entire group was 27 years (28 seminoma, range 19–56; 26 nonseminoma, range 4–56; $P > 0.5$).

Germ cell tumors were localized in 21%, regional in 38%, remote in 35%, and unknown in 6% (Table 2). In treated patients, MED was part or all of treatment in 76% of patients (12/17 seminoma, 14/17 nonseminoma, $P = 0.21$); surgery was part or all of treatment in 50% of patients (6/17 seminoma, 11/17 nonseminoma, $P = 0.48$); and XRT was part or all of treatment in 44% of patients (7/17 seminoma, 8/17 nonseminoma, $P = 0.48$) (Table 3). The overall five-year survival of all malignant germ cell tumors was 51% (62% seminoma vs 40% nonseminoma, $P = 0.08$) (Table 4).

Malignant thymomas occurred in 14% of patients (Table 1). Fifty-eight percent (18/31) were male. Median age was 60 years (range 28–82). Sixteen percent were localized, 48% were regional, 29% were remote, and 7% were unknown (Table 2). In treated patients XRT was part or all of treatment in 70%, surgery was part or all of treatment in 63% patients, and MED was part or all of treatment in 43% (Table 3). The overall five-year survival of thymoma was 49% (Table 4). All patients with localized disease (5/5), and no patient with distant disease (0/9) were alive at five years ($P < 0.001$).

Sarcomas were present in 5% patients (Table 1). Fifty-eight percent (7/12) were male. Median age was 55 years (range 11–77). Fifty-eight percent were localized, 8% were regional, and 33% were remote (Table 2). In treated patients, surgery was part or all of treatment in 89% of patients, MED was part or all of treatment in 67% of patients, and XRT was part or all of treatment in 56% of patients (Table 3). Five-year survival was 33% (Table 4). No patient with regional or distant disease was alive at five years ($P = 0.08$).

Neurogenic tumors were present in only 3% of patients (Table 1). Neuroblastoma was present in 83% and ganglioneuroblastoma in 17%. Thirty-three percent (2/6) were male. Median age was less than 1 year (range 0–55). Fifty percent were localized, 33% regional, and 17% remote (Table 2). In treated patients surgery was part or all of treatment in 100% of patients, XRT was part or all of treatment in 20% of patients, and MED was not used in any patient (Table 3). Five-year survival was 56%. No patient with regional or distant disease was alive at five years ($P = 0.40$) (Table 4).

Other tumors were present in 7% of patients (Table 1). These consisted of malignant neoplasms not otherwise specified in 53% (8/15); mesothelioma and carcinoid tumor, each in 13% (2/15); and squamous carcinoma, carcinoma not otherwise specified, and malignant small cell tumor, each in 7% (1/12). None of these tumors were felt to represent metastatic disease.

Table 5 shows comparisons within the entire series between histologic types. There were significant differences in age and gender ($P < 0.001$), stage at presentation ($P = 0.001$), and in treatment with either MED or surgery ($P < 0.001$). Despite these differences, overall five-year survivals were not statistically different.

Discussion

Primary tumors and cysts of the mediastinum are uncommon: they represent only 1/1076 to 1/3400 admissions to tertiary care medical centers and approximately 3% of tumors within the chest.[1–4] In collected series of primary mediastinal tumors and cysts, 25% to 49% of these lesions are malignant.[1,2,4–13] This group of 219 patients, 0.2% of patients within our registry, represents a large series containing exclusively malignant primary mediastinal neoplasms.

The reported frequency of histologies depends upon the inclusion criteria of the series. Treatment or age selection, inclusion of benign tumors and cysts, and classification by anatomic location, tissue of origin, or pathologic diagnosis will affect results. Our series includes all patients with malignancies diagnosed within New Mexico between 1973 and 1995. Cases were not selected using any of these factors.

The gender distribution was relatively constant with two notable exceptions. Germ cell tumors occurred almost exclusively in males; only 6% of germ cell tumors, and none of the seminomas, developed in females. In contrast, 66% of neurogenic tumors occurred in females. Otherwise, 58% of lymphoma, thymoma, and sarcoma patients were male.

TABLE 5.—*Statistical Comparison Between Histologies (%)*

	Lymphoma	Germ Cell	Thymomo	Sarcama	Neurogenic	P Value
Median age	45	27	60	55	1	<.001
Gender						<.001
Male	69 (57)	32 (94)	18 (58)	7 (58)	2 (33)	
Female	53 (43)	2 (6)	13 (42)	5 (42)	4 (67)	
Stage						.001
Localized	60 (50)	7 (21)	5 (16)	7 (58)	3 (50)	
Regional	22 (18)	13 (38)	15 (48)	1 (8)	2 (33)	
Distant	35 (29)	12 (35)	9 (29)	4 (33)	1 (17)	
Treatment						
Radiation	58 (53)	15 (44)	21 (70)	5 (56)	1 (20)	.15
Chemotherapy	85 (77)	26 (76)	13 (43)	6 (67)	0 (0)	<.001
Surgery	16 (15)	17 (50)	19 (63)	8 (89)	5 (100)	<.001
Survival						
Overall	(54)	(51)	(49)	(33)	(56)	>.50
Localized	(55)	(37)	(100)	(57)	(67)	.33
Regional	(64)	(53)	(62)	(0)	(0)	.40
Distant	(43)	(48)	(0)	(0)	(0)	.02
Total	121	34	31	12	6	

Histology varied notably by age (Figure 1). In the first decade, neurogenic tumors were most common. From the second to fourth decades, lymphoma and germ cell tumors predominated. After the fifth decade, lymphomas and thymomas were most common. Unlike the other tumors, sarcomas were evenly distributed in frequency over the entire age spectrum.

The most common tumor in our series was lymphoma. Other studies have variably reported lymphoma, germ cell tumors, thymoma, and primary mediastinal carcinomas to be the most common malignant primary mediastinal tumors.[1,2,4–8,12,14] Davis et al reported a series containing 166 malignant mediastinal tumors, of which lymphoma was most common and found in 37%.[8] Azarow et al reported the Walter Reed experience: lymphoma was the most common malignancy present in 45% of their 101 recent cases.[6] Cohen and co-workers reported an earlier Walter Reed series of 84 patients with malignant tumors: lymphoma was most common, present in 43% of patients.[7] Ovrum and Birkeland reported 34 malignant lesions of which lymphoma was most frequent and present in 32% of cases.[12] Heimburger et al also reported lymphoma to be the most common malignant histology present in 24% of their 37 cases.[1] Other series of primary mediastinal tumors report lymphoma to be present in 15% to 36% of malignant lesions.[2,4,5,9,11,14,15]

We found Hodgkin's disease in one third of lymphomas and non-Hodgkin's lymphoma in the remainder. Hodgkin's disease, usually nodular sclerosing, has been reported previously in 15% to 86% of mediastinal lymphomas.[4,5,8] Our most common subtypes were nodular sclerosing Hodgkin's and large-cell diffuse malignant lymphoma, each in 26%. Others have also found nodular sclerosing Hodgkin's or large-cell diffuse malignant lymphomas to be the most common subtypes of primary mediastinal lymphomas.[9,10,15,16] Our patients with Hodgkin's disease were significantly younger at presentation, treated more commonly with XRT and less often with MED, and had significantly better five-year survivals than patients with non-Hodgkin's lymphomas.

Mediastinal germ-cell tumors arise from malignant transformation of mediastinal primordial germinal elements. Only 1% to 3% of germ cell tumors occur within the mediastinum; 42% percent to 50% of these tumors are malignant.[3,6,8,–10,13] We found malignant germ cell tumors in 16% of our patients with malignant mediastinal tumors. Wongsangiem reported germ cell tumors in 47% of 62 patients with primary mediastinal malignancy.[4] Adkins and colleagues noted germ cell tumors in 29% of 38 malignant lesions.[5] Other studies have reported germ cell tumors to represent 3% to 14% of primary malignant mediastinal lesions.[1,2,6–9,11–14]

Seminoma is the most common malignant germ cell tumor of the mediastinum and has been reported to occur in 21% to 50% of malignant mediastinal germ cell tumors.[4,5,7,–10,13] We found seminoma in 50% of our patients. Despite all seminoma patients being male, there were no statistical differences between genders of seminomas and nonseminomas. Staging and treatment were also similar, but the five-year survival of 62% for seminomas was better than the 40% for nonseminomas. Other studies have reported overall five-year survivals of 45% for malignant germ cell tumors and 58% to 82% for seminomas.[3,5,8,13]

Malignant thymoma occurred in 14% of our patients. Thymoma was reported by Conkle and Adkins to be present in 26% of 43 patients with malignant lesions.[14] Rubush et al found thymoma in 59% of 61 patients

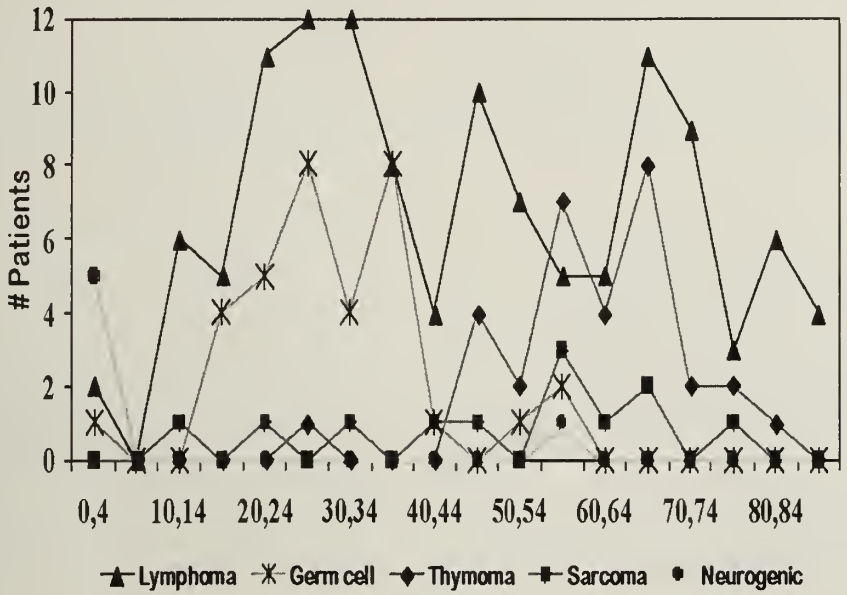


Figure 1.—Frequency of histologic types by age.

reported.[2] Nandi et al reported thymoma in 20% of 26 malignant tumors.[11] Others studies have reported malignant thymomas to represent 11% to 31% of primary malignant mediastinal masses.[1,4–8,12]

Thymomas are classified as malignant when the tumor invades into or beyond the capsule: This is reported in 39% to 46% of cases.[4,8,13] Because no evidence shows intrinsic differences between benign and malignant thymoma, abandoning this classification and considering all thymomas malignant has been recommended.[3,13] Noninvasive thymomas have been shown to have better survival than invasive thymomas. Only invasive thymomas are entered into the SEER registry, resulting in lower total numbers, lower resectability rates, and lower survivals than other reports in the literature. Surgical resection of thymomas has been performed in 82% to 100% of selected cases in previous reports, but only two thirds of our patients received surgery.[4,9,14] We found localized invasive thymoma had a significantly better survival rate than higher-stage invasive thymoma. Inclusion of only higher-stage thymomas resulted in a lower overall survival of 49% at five years than the 65% to 79% previously reported.[5,13,17–19]

We found sarcoma in 5% of our cases. Other studies have reported sarcomas in 2% to 8% of malignant primary mediastinal tumors.[1,2,4,7,8,10–14] Surgery was the primary treatment in 89% of treated patients. Five-year survival was significantly better for patients with localized tumors than for those with higher-stage sarcoma.

Neurogenic tumors are reported to be the most common primary mediastinal tumor in children; rates vary in adult series.[3,6,10,13] Six percent to 28% of these lesions are malignant overall.[8–10] We found malignant neurogenic tumors in 3% of our series. Other studies have reported neurogenic tumors in 2% to 21% of primary mediastinal malignancies.[1–8,10–14] Almost all tumors were neuroblastomas occurring in infants. Surgery was used in all treated patients. Overall five-year survival for our series was 56%, and only patients with localized disease survived.

Seven percent of patients had other, uncommon primary mediastinal malignancies. Others have reported primary carcinoma of the mediastinum in 7% to 30% of tumors.[1,5,7,10,12] Primary carcinoma of the mediastinum is poorly defined, however, and some cases may represent metastatic disease from unknown primaries. Many of these tumors in older series were misdiagnosed prior to the advent of modern pathologic diagnostic techniques.[5]

The prevalence of tumors in our series varied from some previously published reports. The rates of traditionally nonsurgical tumors such as lymphoma and malignant germ cell tumors are higher, and the rates of traditionally surgical diseases such as thymoma and neurogenic tumors are lower. The large number of patients in our study, the modern period under examination, the exclusion of benign tumors and cysts, and the absence of selection bias suggests our results are representative of the actual distribution of malignant mediastinal tumors.

This study demonstrates significant differences in demographics, stage at presentation, and treatment between histologies in a contemporary group of patients with these unusual tumors. Despite these differences, survival rate between histologic groups are not statistically different. The low incidence of these tumors suggests future use of tumor registries, and multi-institutional approaches may improve our experience and understanding of these tumors. The relatively poor five-year survival rate suggest further advances in treatments are needed. Just as with other thoracic malignancies, treatments may take the form of multimodality approaches in the future.

Acknowledgment

We are indebted to our consultant statistician Clifford R. Qualls, PhD, Professor Emeritus, Mathematics and Statistics, University of New Mexico, for invaluable assistance in analysis of data.

REFERENCES

1. Heimburger I, Battersby J, Vellios F. Primary neoplasms of the mediastinum: a fifteen year experience. Arch Surg 1963; 86:120–126

2. Rubush J, Gardner I, Boyd W, Ehrenhaft J. Mediastinal tumors: review of 186 cases. J Thorac Cardiovasc Surg 1973; 65:216–222

3. Silverman N, Sabiston D, Jr. Mediastinal masses. Surg Clin North Am 1980; 60:757–777

4. Wongsangiem M, Tangthangtham A. Primary tumors of the mediastinum: 190 cases analysis (1975–1995). J Med Assoc Thai 1996; 79:689–697

5. Adkins R Jr, Maples M, Hainsworth J. Primary malignant mediastinal tumors. Ann Thorac Surg 1984; 38:648–659

6. Azarow K, Pearl R, Zurcher R, Edwards F. Primary mediastinal masses: a comparison of adult and pediatric populations. J Thorac Cardiovasc Surg 1993; 106:67–72

7. Cohen A, Thompson L, Edwards F, Bellamy R. Primary cysts and tumors of the mediastinum. Ann Thorac Surg 1991; 51:378–386

8. Davis R Jr, Oldham H Jr, Sabiston D Jr. Primary cysts and neoplasms of the mediastinum: recent changes in clinical presentation, methods of diagnosis, management and results. Ann Thorac Surg 1987; 44:229–237

9. Goldberg M, Burkes R. Current management of mediastinal tumors. Oncology 1994; 8:99–111

10. Hoffman O, Gillespie D, Aughenbaugh G, Brown L. Primary mediastinal neoplasms (other than thymoma). Mayo Clin Proc 1993; 68:880–891

11. Nandi P, Wong K, Mok C, Ong G. Primary mediastinal tumors. J R Coll Surg Edinb 1980; 25:460–466

12. Ovrum E, Birkeland S. Mediastinal tumors and cysts. Scand J Thorac Cardiovasc Surg 1979; 13:161–168

13. Rosenberg J. Neoplasms of the mediastinum, In DeVita V Jr, Hellman S, Rosenberg S (Eds). Cancer: Principles and Practice of Oncology. Philadelphia, PA, Lippincott, 1993, pp 759–775

14. Conkle D, Adkins R Jr. Primary malignant tumors of the mediastinum. Ann Thorac Surg 1972; 14:553–567

15. Sutcliffe S. Primary mediastinal malignant lymphoma. Semin Thorac Cardiovasc Surg 1992; 4:55–67

16. Ledermann J. Commentary: lymphoma involving the mediastinum-challenges in diagnosis and management. Thorax 1995; 50:1121–1123

17. Blumberg D, Port J, Weksler B, et al. Thymoma: a multivariant analysis of factors predicting survival. Ann Thorac Surg 1995; 60:908–914

18. Motoyama T, Yamamoto O, Iwamoto H, Watanabe H. Fine needle aspiration cytology of primary mediastinal germ cell tumors. Acta Cytol 1995; 39:725–732

19. Regnard J, Magdeleinat P, Dromer C, et al. Prognostic factors and long-term results after thymoma resection: a series of 307 patients. J Thorac Cardiovasc Surg 1996; 112:376–384

Articles

Physical Fitness, Aging, and Sexuality

WALTER M. BORTZ, II, MD, *Palo Alto, California;* DOUGLAS H. WALLACE, PHD, *San Francisco, California*

Sexuality is a major quality-of-life issue, even into advanced age. Although relatively few studies have addressed sexuality, most studies have emphasized the decline in both sexual performance and satisfaction with aging. In an effort to assess possible positive modifiers of the decline, we included questions concerning sexuality in a multipurpose 90-item questionnaire submitted to members of the Fifty Plus Fitness Association based in Stanford, California. This group is unique in its commitment to a very active lifestyle and has served as a cohort for many prior studies related to fitness and medical outcomes. Sixty-seven percent of the membership returned the mail questionnaire, and 59% of these respondents replied to the sexually relevant items. The results indicated a high level of sexual activity and satisfaction in both older men and women of the Fifty Plus Fitness Association members. Further, sexual satisfaction seemed to correlate with the degree of fitness. We conclude that physical fitness and high levels of sexual activity are mutually supportive elements of successful aging.

(Bortz WM II, Wallace DH. Physical fitness, aging, and sexuality. West J Med 1999; 170:167–169)

Everyone wants to live longer if the latter years are replete with the vitality, virtues, and values of young life. A long life of high functional capacity until the moment before death is the universal ideal.

Conversely, biologic, cognitive, and social decrements clearly cast the prospect of aging in a dim light.[1] One of the most prominent losses is the decline in sexual functioning in older people of both sexes.[2–4] For the male such loss is due predominantly to problems with erectile competence. For the female the loss is tied closely to untreated menopausal conditions and to decreased social opportunity.[5] Both genders identify a desire for more sexual activity than they are experiencing. In other words, what they report as usual is not successful.[6]

Methods

In an effort to characterize behaviors that might improve late-life sexuality, we included questions regarding sexual activity and sexual satisfaction within a 90-item questionnaire submitted to the membership of the Fifty-Plus (50+) Fitness Association, an organization of older persons who are bonded by the pursuit of a physically active mode of life. The association comprises about 2,000 members nationwide, who share a common interest in demonstrating the effects of a physically active lifestyle on the health and well-being of older persons. The age range of the membership is 50–94 years; the average age is 61.7 years. Eighty-five percent of the members are college graduates, and they pursue a wide range of sports activities of which jogging, biking, and walking are most commonly reported. Only a few elite athletes are part of the group. The organization has served as a cohort in numerous major research projects dealing with mortality[7] and several disease states such as cardiovascular, musculoskeletal, and psychologic conditions.

The data reported here are part of a larger longitudinal study funded by the StairMaster Corporation (Kirkland, Washington), in which the 50+ fitness group is coupled with the long-established College Alumni Study under the leadership of Dr Ralph Paffenbarger of the Stanford University School of Medicine and the Harvard School of Public Health.[8] The 50+ group is contrasted with the less-active alumni group in numerous health outcome measurements, some of which are reported elsewhere.[9]

Questions regarding sexuality were included in the questionnaire that was sent to the 50+ fitness group, and these questions allowed an opportunity to generate unique information regarding aging, sexuality, and physical fitness.

The questionnaire was mailed to all members of the 50+ Fitness Association and returned to the office. Sixty-seven percent of the membership returned the questionnaire, and 59% of the 1,039 returned forms contained responses to the sexually related items.

One question requested information on the frequency per week of bouts of intimacy—we presume that

From the Palo Alto Medical Foundation, Stanford University School of Medicine, Palo Alto, California (Dr Bortz); and the Department of Psychiatry, University of California, San Francisco, California (Dr Wallace).

Reprint requests to Walter M. Bortz, II, MD, Palo Alto Medical Foundation, 300 Homer Ave, Palo Alto, CA 94301.

Table 1.—*Frequency of Intimacy and Intercourse Per Week by Age and Sex**

Times Per Week	Aged 50–59 Female (n = 176)	Aged 50–59 Male (n = 178)	Aged 60–69 Female (n = 157)	Aged 60–69 Male (n = 321)	Aged 70+ Female (n = 56)	Aged 70+ Male (n = 134)
0	28% [28%] †	11% [14%]	39% [42%]	16% [21%]	62% [64%]	21% [29%]
<1	19 [22]	16 [27]	20 [27]	28 [36]	10 [20]	25 [35]
1–2	32 [38]	46 [43]	27 [24]	33 [35]	15 [10]	35 [32]
3+	21 [11]	28 [15]	14 [7]	22 [7]	13 [6]	18 [3]
Not applicable	*n* = 26	*n* = 4	*n* = 30	*n* = 14	*n* = 16	*n* = 8

*Survey questions were: "In an average week, how frequently do you have sexual intimacy?" and ". . . how frequently do you have sexual intercourse?"
†Number equals percentage frequency of intimacy of applicable respondents. Brackets represent percentage frequency of intercourse.

intimacy is kissing, hugging, massage, and activities including but not limited to sexual intercourse.

Results

Table 1 shows the weekly frequency of sexual intimacy and intercourse of the 50+ Fitness Association members according to age group and gender. The "not applicable" group represents those without a sexual partner and is excluded from the calculated percentages. A substantially higher percentage of female members lack a partner. Also shown is the high frequency of sexual expression by both sexes: 53%, 41%, and 28% of females reported one or more bout of sexual intimacy per week for the 50–59, 60–69, and 70+ age groups, respectively. The corresponding figures for the males are 74%, 55%, and 53%. The data for sexual intercourse are somewhat less than that for intimacy, yet still reflect robust sexuality even past age 70. For men and women, the frequency of intimacy and intercourse declines with age, but the men have a higher frequency at all ages. Over 60% of the women over 70 report no intimacy or intercourse per week, whereas less than half this percentage (29%) of male respondents do.

Similarly, when degrees of satisfaction with one's sex life were assessed, 44% of all females expressed satisfaction, and 33% expressed dissatisfaction (Table 2). The men reported 61% satisfaction and 29% dissatisfaction. We should note that these calculations include even those with no sexual partners. Presumably, if only those with partners were considered, then the satisfaction percentages would have been higher. Furthermore, the aging process does not seem to affect satisfaction despite a clear decline in frequency both in bouts of intimacy and intercourse.

Discussion

An earlier survey of a smaller number of 50+ Fitness Association members over the age of 70 revealed that 60% of the males (n = 26) rated their sexual activity as good, 28% fair, and 17% poor.[10] Similar figures for the five respondent females over 70 years of age were 40%, 40%, and 20%, respectively.

In an effort to see whether there may be an association between the degree of fitness as estimated by the 50+ Fitness Association members and their frequency of intimacy, we found the data to reveal that improved fitness levels are positively associated with frequency of sexual intimacy. Thirty percent, 38%, and 66% of the females reported one or more bouts of sexual intimacy per week for the least, middle, and most fit groups, respectively. The corresponding figures for the men are 46%, 60%, and 63%. Interestingly, improved fitness also

TABLE 2.—*Satisfaction with Sex Life*

How Satisfied	Aged 50–59 Female (n = 170)	Aged 50–59 Male (n = 182)	Aged 60–69 Female (n = 1497)	Aged 60–69 Male (n = 322)	Aged 70+ Female (n = 48)	Aged 70+ Male (n = 137)
Very	8%	32%	25%	27%	25%	31%
Somewhat	21	37	20	31	6	29
Neither	19	7	20	10	42	13
Dissatisfied	18	14	19	24	19	20
Very dissatisfied	12	10	16	6	7	7

showed a strong postive correlation with the degree of sexual satisfaction in men, but not in women.

We fully acknowledge methodologic limitations of this survey. The respondents are self-selected and are by definition not representative of the community at large. Furthermore, the questions were not statistically validated, and so, the data must be interpreted with this in mind. We did not have a control group; we have, however, sampled a less physically active group drawn largely from the same geographic area, age group, and educational background.

The relationship of sexuality to longevity compels interest. A Swedish study found that males, but not females, who had discontinued intercourse had elevated death rates.[11] Recently, a report titled *Sex and Death: Are They Related?* was published by the Department of Epidemiology and Public Health at the University of Bristol and Queen's University in Belfast and concerns a survey conducted in 1979–1983 of 1,222 men aged 45–59.[12] The group consisted of the entire similar-aged male population of a town, Caerphilly, in South Wales. At recruitment, a standard history and physical examination was carried out and a set of questions regarding frequency of sexual intercourse was asked by a medical interviewer. Seventy-five percent of the men ($n = 918$) responded to the sexuality question. A 10-year follow-up of the respondents revealed that 150 men had died (16%). When age was adjusted, the men who were in the sexually active group had half the mortality of the inactive group, suggesting a dose-response type of relationship. This result is similar to one report by Palmore at Duke, 16 years ago.[13]

The Belfast results were adjusted for social class, blood pressure, smoking, cholesterol, and heart disease history, but physical activity was not considered. Perhaps the survivors were physically active in addition to their increased rate of intercourse, and the exercise may have been the modulator, and the sexuality only an associated factor.[12]

Our study seeks to include physical activity as well as sexuality in the life-span equation. Although we do not have specific mortality data versus the other variables in our group, we know that the overall mortality of the 50+ Fitness Association is only 30% of an inactive control group.[7]

Furthermore, the 50+ group is more sexually active than earlier reports indicated. Establishing causal relationships—whether the greater fitness facilitated more sexual activity, or the reverse, or whether both are reflections of other functions, which are still not understood—is not possible.

The information we mentioned deals largely with men. The story for women may be different. The cited Duke study revealed that female longevity was associated with enjoyment of intercourse rather than its frequency.[13]

The membership of the 50+ Fitness Association has a low incidence of early mortality.[7] They also have been shown, in this study, to have high levels of sexual activity. Therefore, the three dimensions of age, physical activity, and mortality are related. The causal sequence is uncertain. We encourage the clinician to include questions regarding sexuality when taking the medical history of older persons, and if problems are revealed, to suggest that a program of physical exercise may be a valuable prescription.

An editorial in the *British Medical Journal* observed "what we thought was bad for you may actually be good for you, but it may not be good to tell you in case you do it too much, and it is certainly not good to tell you it is good for you if you do too much of it already."[14]

Acknowledgment

The assistance of Theresa Crenshaw, MD, in preparation of the manuscript is gratefully acknowledged.

REFERENCES

1. Branch L, Katz S, Kniepman K. A perspective study of functional status among community elders. Am J Pub Health 1984; 74:266–268

2. Kinsey A, Pomeroy W, Martin G. Age and sexual outlet. In Kinsey A, Pomeroy W, Martin C (Eds). Sexual Behavior in the Human Male. Philadelphia, PA, WB Saunders, 1948, pp 218–262

3. Masters W, Johnson V. Human Sexual Response. Boston, MA, Little Brown & Co Inc, 1970

4. McKinlay J, Brambille D. Where do we go from here? Disentangling aging processes from the processes of aging, chap 12. In Schroots J (Ed). Aging, Health, and Competence. New York, Elsevier, 1993

5. Wiley D, Bortz W. Sexuality and aging—usual and successful. J Gerontol 1996; 51A:M142–M146

6. Rowe J, Kahn R. Human aging—usual versus successful. Science 1987; 237:143–149

7. Fries J, Singh G, Morfeld D, et al. Running and the development of disability with age. Ann Intern Med 1994; 121:502–509

8. Paffenbarger R, Hyde R, Wing A, et al. The association of changes in physical activity level and other lifestyle characteristics and mortality among men. N Eng J Med 1993; 328:538–545

9. Clark T, Bortz W, Behling, et al. Physical activity and aging I. Characteristics of the members of the fifty-plus fitness association. J Aging Phys Activity 1999; in press

10. Bortz W IV, Bortz W II. Aging and the disuse syndrome—effect of lifetime exercise. In Harris R, Harris S (Eds). Physical Activity, Aging, and Sports, Center for the Study of Aging, 1993, Albany, NY, 1993 pp 44–50

11. Persson G. Five-year mortality in a 70-year-old urban population in relation to psychiatric diagnosis, personality, sexuality, and early parental death. J Psychosomatic Res 1980; 24:244–253

12. Smith GD, Frankel S, Yarnell J. Sex and death, are they related? Findings from the Caerphilly cohort study. BMJ 1997; 315:1641–1645

13. Palmore E. Predictors of the longevity difference: a 25-year followup. Gerontologist 1982; 22:513–518

14. Just what the doctor ordered—more alcohol and sex [Editorial]. BMJ 1997; 315:1641–1642

Alerts, Notices, and Case Reports

Alternating Transient Dense Hemiplegia Due to Episodes of Hypoglycemia

MUHAMMAD A. WATTOO, MD
HANS H. LIU, MD, FACP
Philadelphia, Pennsylvania

ACUTE ONSET OF HEMIPLEGIA is a common presentation of cerebrovascular accident. Rapid reversal of this focal neurologic deficit may occur with transient ischemic attacks. However, hypoglycemia has been reported only rarely as a cause of reversible motor deficits. We now report the first case of a patient with alternating right and left dense hemiplegia related to episodes of hypoglycemia.

Report of a Case

A 69-year-old African American male with a medical history of hypertension, congestive heart failure, chronic renal insufficiency, anemia, and myocardial infarction in 1988, was diagnosed as having type II diabetes mellitus. One week prior to admission, he was started on glyburide 5 mg orally once a day. There was no prior history of cerebrovascular insufficiency, migraine headache, or seizure disorder. His family history was noncontributory.

Approximately 18 hours prior to admission, the patient developed gradually worsening slurring of speech and right-sided motor weakness. He initially ignored these symptoms, but on waking up the following morning, he was unable to move the right side of his body. There was no history of nausea, vomiting, headache, trauma to the head or body, chest pains, fever, chills, shortness of breath, or seizure activity associated with this episode. The patient previously had been independent in his daily activities and lived alone without assistance. He drank alcohol socially, but he had stopped smoking eight years before and denied other substance abuse. Medications upon admission were: aspirin 325 mg daily, isosorbide dinitrate 10 mg three times a day, digoxin 0.125 mg daily, furosemide 40 mg daily, hydralazine 25 mg three times a day, and the glyburide.

(Wattoo MA, Liu HH. Alternating transient dense hemiplegia due to episodes of hypoglycemia. West J Med 1999; 170:170–171)

From the Department of Medicine (Dr Wattoo), University of Pennsylvania Health System/Presbyterian Medical Center, Philadelphia, Pennsylvania; and Allegheny University Medical Practices (Dr Liu), Allegheny Health, Education and Research Foundation, Philadelphia, Pennsylvania.

Reprint requests to Hans H. Liu, MD, 219 Garnet Lane, Bala Cynwyd, PA 19004 (e-mail: liuliang@aol.com).

In the emergency room, the patient was alert, oriented, and cooperative with examiners. His speech was slurred, and he was unable to move the right side of his body. Vital signs were: blood pressure 192/88 mm Hg (left arm, supine, without orthostasis); heart rate 85 beats per minute and regular; respiratory rate 22 per minute and unlabored; and temperature 96.8°F. Pulse oximetry revealed an oxygen saturation of 98%, and a fingerstick blood glucose determination was 1.39 mmol/liter (25 mg/dl). The patient was pale and had trace ankle edema bilaterally. His cardiovascular examination was notable for a soft, systolic murmur along the left sternal border and bilateral femoral bruits. There were no carotid bruits. Chest and abdominal examination findings were normal. On neurological examination, his speech was slurred but intelligible, there was right facial weakness, his upper and lower extremity motor strength was 0 of 5 on the right, and his right toe was up-going. The remainder of his cranial nerve examination and sensory and cerebellar function tests were within normal limits.

Laboratory data were: hemoglobin 1.02 mmol/liter, hematocrit, 0.197, mean corpuscular volume 90 fl, white blood cell count 8,100/μl, platelets 200,000/μl, reticulocyte count 0.8%, prothrombin time and partial thromboplastin time within normal limits; urea nitrogen 22.5 mmol urea/liter, creatine 531 μmol/liter, sodium 143 mmol/liter, potassium 4.7 mmol/liter, chloride 120 mmol/liter, bicarbonate 16.2 mmol/liter, anion gap 7 mmol/liter, glucose 1.66 mmol/liter (30 mg/dl), calcium 2.2 mmol/liter, phosphate 1.2 mmol/liter. His liver function tests were within normal limits, but a creatine phosphokinase (CPK) was elevated at 686 U/liter. A digoxin level was 0.62 nmol/liter. Head computerized tomographic (CT) scan did not reveal any abnormalities.

The patient was given two 50-ml ampules of 50% dextrose in water intravenously, and his speech and right-sided motor function returned to normal within 10 minutes.

Following admission, the patient was monitored with telemetry and frequent vital sign determinations. He was given intravenous 5% dextrose in 0.5% saline. Subsequent glucose determinations were in the range of 2.22–5 mmol/liter (40–90 mg/dl). Acute myocardial infarction was excluded by serial cardiac enzyme determinations. After six hours of hospitalization, the patient again developed slurred speech and manifested hemiplegia, this time involving the left side of his body. This episode occurred in the presence of a physician, and a detailed neurologic examination at that time confirmed left facial weakness and dense left hemiplegia. Motor strength was normal on the right side during the second episode. The patient's vital signs were stable, but a fingerstick determination again revealed hypoglycemia with a glucose level of 1.89 mmol/liter (34 mg/dl). Two

50-ml ampules of 50% dextrose in water were administered, and the speech and left-sided neurologic deficit resolved before the second ampule was completely infused. Cardiac telemetry remained normal during the episode. A repeat CT scan of the patient's head was normal as were Doppler studies of his carotid blood flow. The patient subsequently remained asymptomatic and was discharged on his regular medications, except glyburide, to follow up with his primary care physician.

Discussion

Hypoglycemia may result in two categories of symptoms, adrenergic and central nervous system. The former include pallor, sweating, tremors, tachycardia, hunger, and anxiety. Central nervous system symptoms, also called "neuroglycopenia," include headache, dizziness, visual problems, confusion, erratic behavior, convulsions, and loss of consciousness. Motor dysfunction is rarely seen. There can be a stereotypic subset of symptoms with repeated events. None of the above-mentioned symptoms are specific for hypoglycemia, and a broad differential of structural and metabolic etiologic factors exists.

Adrenergic symptoms are usually evident when blood glucose rapidly falls to a low level. This circumstance, however, may not happen in patients with long-standing diabetes. Gradual decline of blood glucose to hypoglycemic levels is also more likely to result in central nervous system dysfunction without an adrenergic component.[1,2]

Many studies in healthy individuals have defined the sequence of events that accompany an insulin infusion and fall in glucose level. Neurologic symptoms generally develop at blood glucose levels below 2.5 mmol/liter (45 mg/dl), and major dysfunction may be expected below 1.1 mmol/liter (20 mg/dl). In diabetics, considerable variation may be seen depending on chronicity of the disease and prior control of blood sugar component.[1]

Reversible or irreversible hemiparesis is a recognized but rare symptom of neuroglycopenia.[3] A clinical review of 29 documented cases by Forster and Hart indicated that 75% of patients were on insulin and 14% were on oral agents for blood glucose control.[4] Right hemiparesis was more common than left-sided involvement. Episodes could reoccur on the same side and last for a few hours or even days. An elderly population with a previous history of cerebrovascular accident was more likely to be afflicted.

The mechanism of hypoglycemic hemiplegia has not been well-documented. The brain is a highly metabolic organ, which uses glucose as its exclusive energy source. Under hypoglycemic conditions, the energy demand is met by oxidation of cerebral lipids and proteins and may result in brain damage.[5] Several theories may explain the pathogenesis of a hypoglycemia-associated motor deficit. Structural narrowing of blood vessels that supply a particular portion of the brain could result in even lower levels of glucose during generalized hypoglycemia.[6] Angiographic studies, however, have failed to support this theory.[7] Hypoglycemia may act on a cerebral vasomotor center to cause vasospasm in the smaller cortical vessels.[5,7] A third theory attributes local vulnerability to hypoglycemia to differences in cellular metabolism and vascular supply. Both clinical and anatomic studies have demonstrated this theory, but the studies do not completely explain the phenomenon.

Conclusions

In the case presented, hypoglycemia was likely the result of an exaggerated effect of glyburide due to diminished renal clearance. The patient's central nervous system deficits were rapidly reversible by the administration of intravenous glucose. Results of carotid Doppler studies and two computerized tomograms of his head were negative for structural lesions. Finally, alternation of the side of the body involved in two closely occurring episodes of hypoglycemia suggest that vascular spasm and/or differences in local metabolism rather than fixed anatomic lesions may have played a role in our patient's symptoms.

We conclude that hypoglycemia should be considered in the differential diagnosis of any patient presenting with a change in mental status or central nervous system deficits. This includes patients with significant focal neurologic deficits such as hemiparesis/hemiplegia, which would generally be considered signs of cerebrovascular compromise. As in the presented case, hypoglycemia and its sequelae may be rapidly reversed if diagnosed early. Awareness of the possibility of hypoglycemia may be extremely important in diagnosing patients who are unable to provide any medical history upon initial encounter.

If hypoglycemia is suspected as the cause of neurologic deficits, 10–20 ml of blood should be drawn beyond that needed for glucose determination and routine investigations. Additional analysis, including insulin, C-peptide, cortisol, and sulfonylurea levels, can then be determined as appropriate. Other tests, such as carotid Doppler studies, computed tomography, magnetic resonance imaging, or positron emission tomography of the head, or angiography, may be indicated for further evaluation.

REFERENCES

1. Palardy J, Havrankova J, Lepage R, et al. Blood glucose measurement during symptomatic episodes in patients with suspected postprandial hypoglycemia. N Engl J Med 1989; 321:1421–1425

2. Service FJ. Hypoglycemias. J Clin Endocrinol Metab 1993; 76:269–272

3. Pazevic JP, Hambrick RL, Roskam SA. Hypoglycemic hemiplegia. J Am Osteopath Assoc 1990; 90:539–541

4. Foster JW, Hart RG. Hypoglycemic hemiplegia: two cases and a clinical review. Stroke 1987; 18:944–946

5. Siesjo BK, Inguar M, Pelligrino D. Regional differences in vascular autoregulation in the rat brain in severe insulin-induced hypoglycemia. J Cerebr Blood Flow Metab 1983; 3:478–485

6. Portnow HD. Transient 'ischemic' attacks produced by carotid stenosis and hypoglycemia. Neurology 1965; 15:830–832

7. Wallis WE, Donaldson I, Scott RS, et al. Hypoglycemia masquerading as cerebrovascular disease. Ann Neurol 1986; 1:178–186

Pathologic Fracture Occurring 22 Years After Diagnosis of Hairy Cell Leukemia: Case Report and Literature Review

KENNETH S. SNELL, MD
M. MARGARET O'BRIEN, MD
KARLA SENDELBACH, MD
ROY MARTINO, MD
Mobile, Alabama

HAIRY CELL LEUKEMIA (HCL) is a chronic B-cell lymphoproliferative disorder that accounts for approximately 2% of all leukemias.[1,2] The typical clinical picture consists of a man with a median age of between 50 and 55 years with splenomegaly, a varying degree of pancytopenia without lymphadenopathy, and characteristic hairy cells in peripheral blood and bone marrow.[1,2] Bone lesions, having an incidence of 3%, are an uncommon complication of HCL.[1,3] We present a patient who developed a pathologic fracture 22 years after his initial diagnosis. We also provide a review of the literature on this rare complication of HCL.

Case Report

The patient is a 67-year-old man first diagnosed with HCL in November 1973. He underwent splenectomy in January 1974, and was treated with single-agent, chlorambucil therapy from November 1979 to February 1981. His HCL therapy was reinitiated in April 1988, with interferon alpha-2b and was discontinued in July 1989, after achieving an impressive partial response in the abdominal lymph nodes on computed tomographic (CT) scan. Evidence of recurrent disease in the abdominal lymph nodes led to the reinitiation of interferon alpha-2b therapy in December 1990. This therapy was continued until December 1992, when the patient made an informed decision to discontinue the interferon alpha-2b therapy, despite having achieved another partial response in the abdominal lymph nodes.

On July 1 1996, while working on his lawnmower, the patient noted a severe, sharp, stabbing pain in the right proximal leg. The pain started just above the knee and spread to involve the area between the groin and the knee. The patient went to his primary care physician and was referred to a neurologist, who diagnosed a painful mononeuropathy. The patient developed proximal leg weakness and swelling of the right leg and foot over the ensuing month. On July 12, 1996, a CT scan of the chest, abdomen, and pelvis showed no changes to suggest progressive HCL. Laboratory evaluation on July 16, 1996, showed a normal serum calcium of 2.35 mmol/liter (reference: 2.15–2.50 mmol/liter) and a normal serum-alkaline phosphatase of 72 U/liter (reference: less than 250 U/liter).

On August 1, 1996, the patient was sent to the University of South Alabama Medical Center for oncologic evaluation. On physical examination, the patient's right leg was extremely tender to palpation, particularly in the area of the proximal femur. The range of motion of the right hip joint was severely limited by pain. The patient was unable to bear weight on his right leg. No peripheral lymphadenopathy was noted on examination. Anteroposterior radiograph of the right pelvis and femur (Figure 1) showed shortening of the neck of the femur with overlap, which is consistent with a femoral neck fracture. A cemented bipolar arthroplasty was subsequently performed on the right hip. At the time of surgery, the greater trochanter was found to be separated from the femoral neck. The proximal femur was noted to be grossly tumorous. A large mass was removed from the proximal femur and greater trochanter. Pathologic evaluation of the specimen found a leukemic infiltrate completely filling the marrow space in the femoral head and present in fragments of the femoral neck. The leukemic infiltrate abutted thinned, bony trabeculae and areas of necrosis (Figure 2). Flow cytometry studies revealed a monoclonal, B-cell population positive for HLA-DR, CD45, CD19, CD20, CD22, and, most significantly, CD11c and CD25. The population showed kappa light chain restriction. The leukemic infiltrate also had the cytologic features of HCL. Immunohistochemical stains for acid phosphatase and for tartrate-resistant acid phosphatase were positive on the tumor cells.

The patient received no further treatment and recovered without further complications. A bone scan in November 1997 showed no abnormalities aside from the patient's right hip replacement. As of June 1997, the patient continued to do well, with no further complaint of bony pain and no further treatment for his HCL as of that time.

Discussion

We found 32 patients with bony complications of HCL reported in the English literature,[3-17] as well as others reported in the non-English literature.[18-21] The frequency of these complications is reported to be between 0%[22] and 13%.[9] The largest case study reported an incidence of 3%, or in 8 of 267 HCL patients.[3] In contrast, multiple myeloma has a bone lesion frequency of 79%,[23] and other malignant lymphomas have an intermediate frequency of about 27%.[24] The first 3 documented cases of osteolytic bone lesions in HCL patients were presented in 1977.[4] These patients had been diagnosed with HCL two to three years prior to the publication of the report, and two out of the three patients had lesions located in the femoral neck region. The interval between diagnosis of HCL and develop-

(Snell KS, O'Brien M, Sendelbach K, Martino R. Pathologic fracture occurring 22 years after diagnosis of hairy cell leukemia. West J Med 1999; 170:172–174)

From the Departments of Pathology (Drs Snell, O'Brien, and Sendelbach) and Internal Medicine (Dr Martino), University of South Alabama, Mobile, Alabama.

Reprint requests to Kenneth S. Snell, MD, Department of Pathology, University of South Alabama, 2451 Fillingim Street, Mobile, AL 36617-2293.

Figure 1.—This anteroposterior radiograph of the right proximal femur demonstrates a shortening and angulation (white arrow) of the neck of the femur with overlap consistent with a femoral neck fracture.

ment of bony lesions can vary greatly. The lesion can be the initial symptom of HCL[3,7,11,16,17] or may not present for up to 73 months.[3] Our patient presented 22 years after his diagnosis, which is the longest documented interval between a diagnosis of HCL and the development of a bone lesion. This case demonstrates the need for diligent long-term follow-up of cancer patients by their primary care physicians. Localized pain is common to all documented cases, but the pain may precede skeletal roentgenographic abnormalities.[5,6,8,14,17] Laboratory evaluation of the documented patients revealed normal serum calcium and alkaline phosphatase levels, and the same results were obtained in the case we are presenting. A few documented cases have reported alkaline phosphatase elevations associated with the liver instead of bone.[4,7,8,14]

The HCL-associated bony lesions have a predilection for the axial skeleton, with the femoral head, neck, or both accounting for 24 in 31, or about 77% of the cases. This also holds true for the case we are presenting. Other sites include the skull, vertebrae, ribs, humerus, pelvis, tibia, and fibula. As in the present case, the right side is predominantly affected by the lesions. Reported skeletal roentgenographic abnormalities occurred in five different patterns. The predominant pattern is that of an osteolytic lesion occurring in about 77% of the cases (24 of 31).

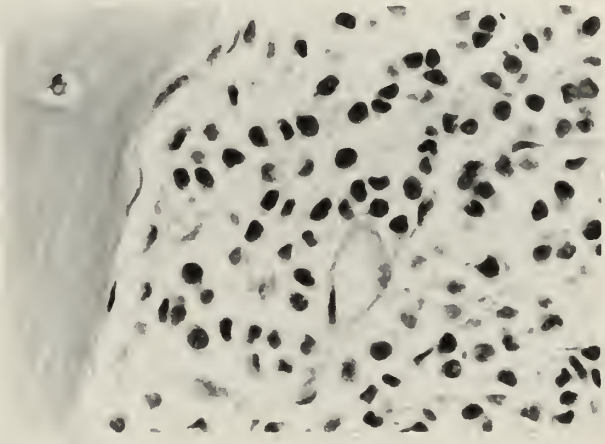


Figure 2.—A medium-high-power view of the femoral neck shows marrow space (adjacent to a bony trabeculae) completely replaced with a uniform population of cells. These cells have nuclei slightly larger than mature lymphocytes and delicate, "feathery" cytoplasm. These are the "hairy cells."

The lesions can present with either well-defined or poorly-defined margins. Diffuse demineralization of the bone is the next most common pattern, reported in 5 of 31 cases.[9,14,17,18] The demineralization can be widespread, local, or associated with an osteolytic lesion. Demeter and colleagues[17] presented two patients complaining of bone pain, both of whom had demineralization lesions and overall decreased bone density. Osteosclerosis occurs infrequently—only four cases have been reported—and presents in a diffuse pattern.[14,16,18] Hudson and colleagues[18] reported an increased bone density associated with the osteosclerotic lesion. Isolated necrosis of the femoral head has been reported in three cases and was the direct cause of a fracture in two of the cases.[3,9,17] Osteoblastic lesions occur least frequently; there are only two reported cases.[7,14] In both cases, the lesion was focally osteolytic, creating a mixed pattern.

In all reported cases, no cortical bone destruction or periosteal reaction was documented. Marcelli and colleagues[15] did report abnormal bone remodeling and a significant increase in bone resorption in three cases.

In the evaluation of bone pain, skeletal roentgenographic studies are the most commonly used technique. Bone scans have been reported to be very effective in supporting roentgenographic findings and have been reported to document lesions when roentgenographic studies were normal.[3,16,23] A positive bone scan shows increased, radionuclide uptake in the area of bony involvement. Magnetic resonance imaging (MRI) scans with T1-weighted images have been used increasingly to confirm lesions found on both roentgenographs and bone scans.[13,14] The MRI scans show non-homogeneous decreases in signal intensity, which are interpreted as hairy-cell infiltration. In the future MRI scans may be used to evaluate further those patients who have multiple areas of bone pain and normal-appearing roentgenographs.

Treatment of the patient with HCL bony involvement has been most successful with radiotherapy. The rad level has varied from 1,500[3] to 6,000,[4] with 2,000 to 3,000 being the most common level used. Interferon alpha has been the most commonly used chemotherapeutic agent, and the results are well documented. Arkel and colleagues[10] also reported improvement in bone pain and roentgenograph abnormality with prednisone therapy alone.

In summary, our 67-year-old patient presented with bony involvement by HCL 22 years after HCL diagnosis and 3.5 years after his cessation of interferon-alpha treatment for HCL. This is the longest documented period between HCL diagnosis and subsequent bony involvement by the disease. This case demonstrates the need for diligent, long-term observation of HCL patients by primary care physicians and other health care professionals. Any complaint of bone pain by a patient with a hematological cancer should be evaluated fully with radiographic methods.

REFERENCES

1. Hess CE. Hairy cell leukemia, malignant histiocytosis, and related disorders. In Lee GR, Bithell TC, Roerster J, Athens JW, Lukens JN (Eds): Wintrobe's Clinical Hematology. Philadelphia, PA, Lea & Febiger, 1993, pp 2170–2180

2. Golomb HM, Vardiman J. Hairy-cell leukemia. In Holland JF, Bast RC Jr, Morton DL, Frei E III, Kufe DW, Weichselbaum RR (Eds): Cancer Medicine. Baltimore, MD, Williams-Wilkins, 1997, pp 2719–2728

3. Lemhersky BX, Ratain MJ, Golomb HM. Skeletal complications in hairy cell leukemia: Diagnosis and therapy. J Clin Oncol 1988; 6:1280–1284

4. Turner A, Kjeldsberg CR. Hairy cell leukemia: A review. Medicine 1978; 57:477–499

5. Rosenthal RL, Steiner GC, Golub BS. Hairy cell leukemia: Historical aspects and bone involvement. Mt Sinai J Med 1979; 46:237–242

6. Demanes DJ, Lane N, Bechstead JH. Bone involvement in hairy-cell leukemia. Cancer 1982; 49:1697–1701

7. Jansen J, Bolhuis RLH, van Nieuwhoop JA, Schuit HRE, Stenfert Kroese WF. Paraproteinaemia plus osteolytic lesions in typical hairy cell leukemia. Br J Haematol 1983; 54:531–541

8. Quesada JR, Keating MJ, Libshitz HI, LLamas L. Bone involvement in hairy cell leukemia. Am J Med 1983; 74:228–231

9. Arkel YS, Lake-Lewin D, Savopoulos AA, Berman E. Bone lesions in hairy cell leukemia: A case report and response of bone pains to steroids. Cancer 1984; 53:2401–2403

10. Keidan AJ, Liu Yin JA, Gordan-Smith EC. Uncommon complications of hairy cell leukemia. Br J Haematol 1984; 57:176–177

11. Westbrook CA, Golde DW. Clinical problems in hairy cell leukemia: Diagnosis and management. Semin Oncol 1984; 11(4, Suppl 2):514–522

12. Peterson C, Kaplan PA, Lorenzen KM. Case report 410. Skeletal Radiol 1987; 16:82–86

13. Herold CJ, Wittich GR, Schwarzzinger I, et al. Skeletal involvement in hairy cell leukemia. Skeletal Radiol 1988; 17:171–175

14. Marcelli C, Chappard D, Rossi JF, et al. Histologic evidence of an abnormal bone remodeling in B-cell malignancies other than multiple myeloma. Cancer 1988; 62:1163–1170

15. VanderMolen LA, Urba WJ, Longo DL, Lawrence J, Gralnick H, Steis RG. Diffuse osteosclerosis in hairy cell leukemia. Blood 1989; 74:2066–2069

16. Demeter J, Grote HJ, Horvath C, et al. Bone densitometry and histomorphometry in patients with hairy cell leukemia. Leukemia Lymphoma 1994; 14(Suppl 1):73–77

17. Hudson J, Cobby M, Yates P, Watt I. Extensive infiltration of bone with marrow necrosis in a case of hairy cell leukaemia. Skeletal Radiol 1995; 24:228–231

18. Rhyner K, Streuli R, Kistler GS. Haarzell-leukämie (hairy-cell leukemia) mit osteolytischen knochenveränderungen. Schweiz Med Wochenschr 1977; 107:863–871

19. Weh HJ, Katz M, Bray B, Rodat O, Degos L, Flandrin G. Bone lesions in hairy cell leukaemia. Nouv Presse Med 1978; 8:2253–2254

20. Bastien P, Huaux JP, Noel H, Nagant de Deuxchaisnes C. Tricholeukocyte leukemia complicated by osteolytic lesions. Rev Rhum Mal Osteoartic 1984; 51287–51288

21. Huaux JP, Noel H, Bastien P, Doyen C, Nagant de Deuxchaisnes C. Bony lesions in hairy cell leukemia: various therapeutic considerations apropos of a case report. Acta Clin Belg1984; 39:339–351

22. Bouroncle BA. Leukemic reticuloendotheliosis (hairy cell leukemia). Blood 1979; 53:412–436

23. Kyle RA. Subject review: multiple myeloma, review of 869 cases. Mayo Clin Proc 1975; 50:29–40

24. Canellos GP. Hypercalcemia in malignant lymphoma and leukemia. Ann NY Acad Sci 1974; 230:240–245

Endotracheal Intubation and Mechanical Ventilation Following Respiratory Arrest From High Altitude Pulmonary Edema

JAMES A. LITCH, MD, DTMH
Solukhumbu District, Nepal

High altitude pulmonary edema (HAPE) is a severe form of altitude illness occurring in some inadequately acclimatized individuals as a result of rapid ascent to high altitude. HAPE is a noncardiogenic pulmonary edema that may be rapidly fatal and can occur with or without prodromal symptoms. Fast recovery is common, however, with early recognition and descent to a lower altitude.[1]

Endotracheal intubation and mechanical ventilation are indicated in a variety of pulmonary, cardiovascular, and neurologic disorders to optimize ventilation and oxygenation as well as protect the airway.[2] The role of prehospital intubation in the management of severe HAPE has not been previously discussed in the literature. This report presents a case of persistent HAPE that resulted in cardiopulmonary arrest following a 2,300 meter descent. The case was managed with endotracheal intubation and manual mechanical ventilation performed

(Litch JA. Endotracheal intubation and mechanical ventilation following respiratory arrest from high altitude pulmonary edema. West J Med 1999; 170:174–176)

From the Himalayan Rescue Association, Kathmandu, Nepal.

Reprint requests to James A. Litch, MD, DTMH, Kunde Hospital, c/o The Himalayan Trust, PO Box 224, Kathmandu, Nepal (e-mail: jlitch@yahoo.com).

while the patient was in a remote area of the Nepal Himalaya.

Report of a Case

A 38-year-old Sherpa man, who was employed as a high-altitude porter for a commercial expedition and had a history of HAPE on a previous expedition, ascended from his resident altitude of 2,900 meters to the 5,300-meter base camp over 7 days. After residing in base camp for 3 weeks with frequent load carries up to 6,500 meters, the patient moved to 6,500 meters to work on improvements to the higher altitude camp. Over the subsequent 48 hours he was noted by teammates to be "lazy," "sitting around," and "not doing his share of work," but he did not descend despite advice by team members to do so. On the third evening at this camp, the patient was noted to be confused and short of breath with a persistent cough productive of pink froth. Teammates suspected that he was suffering from life-threatening HAPE. After the patient received nifedipine and dexamethasone and was started on oxygen therapy, he was taken back to base camp—a dangerous 7-hour night descent.

The patient arrived at the 5,300 meter base camp before midnight, and was examined by the expedition physician, who diagnosed severe HAPE. The patient was continued on nifedipine and dexamethasone, and remained on oxygen overnight. In the morning, the patient had not improved, and an attempt to walk him to a lower elevation failed when he collapsed just outside base camp. The patient refused continued oxygen administration or hyperbaric therapy, arguing that he did not have altitude sickness. By evening the patient still had not improved, despite being at an altitude at which he had resided for over 3 weeks without symptoms. After further medical consultation, oxygen therapy was restarted and antibiotic administration begun, and nifedipine and dexamethasone were continued. A helicopter evacuation was arranged for the following morning, but bad weather precluded the flight early the next day. A strenuous ground evacuation was begun. This descent to Pheriche at 4,200 meters required 12 hours. The patient sat upright in a basket carried by porters and was attended by the expedition physician.

Upon arrival to a lodge at Pheriche, the patient was alert when aroused, and notably tachypnic with a persistent cough. His respiratory rate was 38 breaths per minute, with an oxygen saturation (SaO_2) of 70% on 4 liters per minute oxygen via face mask. Rales were auscultated throughout both lung fields. The patient was placed supine in a portable hyperbaric chamber at 104 mm Hg above ambient barometric pressure for 1 hour. During the hyperbaric therapy, the patient experienced an apparent cardiopulmonary arrest, eventually noticed by a Sherpa who was managing the foot pump. After several minutes of cardiopulmonary resuscitation, the patient was intubated with equipment and assistance from the nearby Pheriche Aid Post, and return of a regular pulse was noted. A decision was made to sedate the patient and continue intubation and ventilation using an ambu bag with oxygen, given the difficulty of the intubation and the protracted course of HAPE over the previous 5 days, despite the 2,300 meter descent. Due to poor weather, helicopter evacuation to Kathmandu was delayed for 40 hours. Manual ventilation, sedation, and monitoring of SaO_2 above 92% were continued. On the third day after admission to the hospital in Kathmandu, the patient was extubated without difficulty. His neurologic function remained markedly impaired, and the patient died in the hospital 2 months later.

Discussion

HAPE is a life-threatening emergency that requires early recognition and treatment. The consequences of delayed recognition, a lack of prompt action, and inadequate/inappropriate treatment are illustrated by this case. The complexity of this case of HAPE, which persisted despite eventual descent, and the subsequent tragic outcome call attention to the difficulties faced when managing emergencies at moderate and extreme altitude.

Oxygen administration and portable hyperbaric chamber treatment are adjuncts to, but not substitutes for, immediate descent to a lower altitude if feasible. HAPE typically resolves rapidly with descent. Descent of 500 meters to 1,000 meters is usually adequate,[3] but descent should continue until symptoms resolve. Signs and symptoms occurring at high altitudes with *1)* atypical onset, *2)* unusual combinations, or *3)* persistence after descent, have been described as indicators of possible diagnoses other than altitude illness.[4] In this case, the lack of improvement after the initial 1,200-meter descent to base camp, where the patient had been previously well, indicates the possibility of more than a simple case of HAPE.

Other underlying conditions might be suggested to have complicated this case of persistent HAPE. Common pulmonary disorders that accentuate hypoxemia through worsening alveolar gas exchange from areas of shunt include pneumonia, pulmonary tuberculosis, pulmonary embolism, cardiogenic pulmonary edema, and acute respiratory distress syndrome (ARDS). ARDS resulting from HAPE has been reported.[5] The presence of such primary- or co-morbidity could complicate expected resolution by descent of suspected HAPE. These conditions would have been unlikely to reverse after only 12 hours of mechanical ventilation, however, and are therefore unlikely to have been present in this case, as evidenced by the clearing of the lungs and markedly improved SaO_2.

In this case of severe HAPE, descent was delayed for several days. After 5 days of severe tachypnea following the onset of HAPE, the patient experienced respiratory failure and subsequent cardiopulmonary arrest after eventual descent totaling 2,300 meters. The author postulates that the cardiopulmonary arrest

resulted from prolonged respiratory insufficiency due to delayed early treatment resulting from lack of recognition of HAPE, further delayed descent when symptoms did not resolve at base camp as expected, and unnoticed clinical deterioration after electing to substitute continuous oxygen administration for hyperbaric chamber therapy in which the patient was laid flat. Continued hypoxemia from respiratory insufficiency due to fatigue and persistent pulmonary edema may have prevented clearing of HAPE despite subsequent descent, leading to respiratory failure as the cause of the cardiopulmonary arrest.

Hypoxic-ischemic encephalopathy likely occurred as a result of the initial delay in detecting the cardiopulmonary arrest during portable hyperbaric chamber therapy. This delay ensued because patients cannot easily be managed in a portable hyperbaric chamber. Oxygen therapy has been found to be equally as effective as hyperbaric therapy in moderate to severe HAPE,[6] and allows ease of access for monitoring the patient. Large quantities of oxygen, however, are not easily available in remote areas. One solution to this problem is the use of a portable hyperbaric chamber matched with the use of continuous-pulse oximetry monitored through the chamber window.

The role of prehospital endotracheal intubation and manual mechanical ventilation in acute respiratory arrest from HAPE alone is unclear. The pulmonary oxygen diffusion impairment, secondary to such a severe degree of pulmonary edema, would be unlikely to improve from manual mechanical ventilation alone (without positive end expiratory pressure); thus significant improvement in gas exchange and oxygenation is unlikely. In the case of respiratory insufficiency/arrest due to fatigue and pulmonary edema, however, such as that suspected in this prolonged case of HAPE, ventilatory support might be argued for in order to improve oxygenation by increasing the fraction of inspired oxygen and converting previous areas of shunt to areas of gas exchange. The difficulties of managing a critically ill patient with endotracheal intubation and manual mechanical ventilation are monumental in the protracted prehospital setting of very remote areas. Oxygen saturation monitoring provides guidance regarding blood oxygenation, but information concerning the effectiveness of the ventilation, specifically the acid–base status, is conspicuously lacking.

Conclusion

Although HAPE can be easily reversible if it is recognized early and prompt descent is undertaken, HAPE can be fatal if unrecognized or ignored. The need for early recognition of HAPE as a respiratory emergency at high altitude, prompting immediate descent, may be underappreciated by some physicians. Ultimately, the responsibility for prevention and early recognition of altitude illness rests with the high altitude sojourners themselves. Often, the greatest threat facing climbers is their own failure to accurately assess a dangerous situation and respond appropriately.[7]

A patient's failure to improve after initial descent must alert the care provider to consider additional causes of pulmonary compromise, while continuing descent, rest, oxygen therapy, and evacuation efforts. Further descent can only help any illness at high altitude. Oxygen administration has the benefit of easier patient monitoring and access compared to portable hyperbaric chambers. Chambers also force the patient into a supine position although this can be overcome by propping up the head of the inflated chamber. Prehospital endotracheal intubation and mechanical ventilation may be considered in the management of acute respiratory failure following HAPE and other emergencies in remote settings.

REFERENCES

1. Schoene RB. Pulmonary edema at high altitude. Review, pathophysiology, and update. Clin Chest Med 1985; 6:491–507

2. Tobin MJ. Mechanical ventilation. N Engl J Med 1994; 330:1056–1060

3. Hackett PH, Roach RC. High altitude pulmonary edema. J Wild Med 1990; 1:3–26

4. Litch JA, Basnyat B, Zimmerman M. Subarachnoid hemorrhage at high altitude. West J Med 1997; 167:180–181

5. Zimmerman GA, Crapo RO. Adult respiratory distress syndrome secondary to high altitude pulmonary edema. West J Med 1980; 133:335–337

6. Hackett PH, Roach RC, Goldberg S, et al. A portable fabric hyperbaric chamber for the treatment of high altitude pulmonary edema. In Sutton JR, Coates G, Remmers JE (Eds). Hypoxia: The Adaptions. Philadelphia, PA, BC Dekker, 1990, p 291

7. Litch JA. Safety at extreme altitude. Wild Envir Med 1996; 7:259–260

Editorial

Identifying Infectious Diseases in Prisons: Surveillance, Protection, and Intervention

More than 1.75 million people, about 1% of the US population, are estimated to be in jails or prisons.[1] Compared to the general population, incarcerated persons have disproportionately high rates of a number of infections, including human immunodeficiency virus (HIV), hepatitis B virus (HBV), tuberculosis, and sexually transmitted diseases.[2–5] The prison is a setting in which persons are accessible and can be enumerated for disease surveillance. This accessibility, however, must be balanced by overriding concerns for the protection of this population, protection that is necessary because of the inherent nature of the prison setting.

Since 1976 (*Estelle v Gamble,* 429 97 [US 1976]), every jurisdiction is responsible for providing health care to its prisoners. Standards for care are provided by such agencies as the National Commission on Correctional Health Care,[6,7] but screening for infectious diseases such as HBV and HIV and the availability and use of follow-up services varies considerably among jurisdictions and facilities.[2,8] For example, in a recent survey, the California State Prison System reported testing for HIV in the following circumstances: at the request of the prisoner, for clinical indications, and following involvement in an incident. Other states in the survey reported a variety of circumstances for HIV testing, from testing all inmates to testing random samples of inmates.[2] Because of a law passed in 1988 in California, correctional medical personnel are required to provide lists of known or suspected HIV-positive prisoners to correctional staff. Voluntary testing for HIV, identification of HIV status, and engagement in HIV-related care by persons entering prison may be influenced by perceptions of discrimination as well as the reality of prison officials using this information to make decisions about housing and segregation, work assignments, and visiting privileges.

In light of the evidence of high prevalence in their sample, Ruiz and his colleagues conclude that risk factor evaluation at entry and inmate education and counseling are important in preventing HIV, HBV and hepatitis C virus (HCV) infections.[9] For HBV, the availability of vaccination enables correctional medical personnel to encourage screening of appropriate target groups, and standards for care encourage the provision of vaccination to susceptible persons, and education and counseling to those who are seropositive.[7,8]

Opportunities for therapeutic intervention exist, but so do dilemmas in providing therapies in prison. There are promising studies of medical interventions among HIV-positive prisoners,[10] and work is under way to identify specific groups that would benefit from treatment with interferon for HCV.[11] Inmates may stay long enough to complete a course of therapy for certain infectious diseases. In the case of chronic conditions that require long-term or even lifelong therapy, however, the correctional facility represents a starting point for care that must be continued after release. A number of models of interaction between correctional health and public health have demonstrated the benefits of collaboration to improve the continuity of care between the correctional facility and the community.[12]

Prison and jail inmates have disproportionately high rates of a number of infectious diseases related to both socioeconomic factors and risk behaviors of this group. Studies such as that of Ruiz et al are important contributions to understanding the epidemiology of disease by estimating the magnitude among high-risk groups.[9] Although the prison population is a sentinel site for surveillance, the nature of incarceration and prison life emphasize the necessity for protection. As more and improved therapies emerge, screening may be more widespread in prisons, thereby increasing the ability to identify persons who would benefit from therapy or interventions to reduce the risk of disease. Correctional health care systems may be the setting for initiation of care that, in combination with public health and community care, has an important positive impact on the lives of prisoners.

MARY CASTLE WHITE, RN, MPH, PhD
Associate Professor
University of California, San Francisco

REFERENCES

1. Gilliard DK, Beck AJ. Prison and jail inmates at midyear 1997. Bureau of Justice Statistics Bulletin, January, 1998. Washington, DC, US Department of Justice, NCJ 167247

2. Marushak L. HIV in prisons and jails, 1995. Bureau of Justice Statistics Bulletin, August, 1997. Washington, DC, US Department of Justice, NCJ 164260

3. Centers for Disease Control and Prevention. HIV/AIDS education and prevention programs for adults in prisons and jails and juveniles in confinement facilities—United States, 1994. MMWR Morbid Mortal Weekly Rep 1996; 45:268–271

4. Wilcock K, Hammett TM, Widom R, Epstein J. Tuberculosis in correctional facilities 1994–1995. Research in Brief. Washington, DC, US Department of Justice, July, 1996

5. Centers for Disease Control and Prevention. Prevention and control of tuberculosis in correctional facilities: recommendations of the Advisory Council for the Elimination of Tuberculosis. MMWR Morbid Mortal Weekly Rep 1996; 45:1–26

6. Mumola CJ. Substance abuse and treatment, state and federal prisoners, 1997. Bureau of Justice Statistics Bulletin, January, 1999. Washington, DC, US Department of Justice, NCJ 172871

7. National Commission on Correctional Health Care. Standards for Health Services in Prisons. Chicago, Ill, 1997

8. National Commission on Correctional Health Care. Standards for Health Services in Jails. Chicago, Ill, 1996

9. Ruiz JD, Molitor F, Sun RK, et al. Prevalence and correlates of hepatitis C virus infection among inmates entering the California correctional system. West J Med 1999; 170:156–160

10. Inciardi JA. HIV risk reduction and service delivery strategies in criminal justice settings. J Subs Abuse Treat 1996; 13:421–428

11. Wong JB, Bennett WG, Koff RS, Pauker SG. Pretreatment evaluation of chronic hepatitis C. JAMA 1998; 280:2088–2093

12. Hammett TM. Public health/corrections collaborations: prevention and treatment of HIV/AIDS, STDs, and TB. Research in Brief. Washington, DC, National Institute of Justice, July, 1998

Correspondence

Cigarette Smoking Prevention—Physicians Should Teach by Example

To the Editor: The article in the July issue on the clinician's role in cigarette smoking prevention, by Pérez-Stable and Fuentes-Afflick,[1] reviewed guidelines for clinicians who provide care to children in preventing the onset of tobacco use, counseling parents of children who smoke, and counseling adolescents who have started smoking. But the authors failed to mention one most important guideline that clinicians should follow in preventing cigarette smoking—the clinicians should set the example by not smoking themselves.

In addition to the five A's—anticipate, ask, advise, assist, and arrange—developed by the National Cancer Institute to target physicians caring for children,[2] there should be a sixth A—abstain. Advising patients not to smoke would be extremely difficult if physicians walk into the exam room with the smell of cigarette smoke on their coats or breath, yellow stains on their fingernails, or other telltale signs of smoking. Therefore, physicians must abstain from smoking before they can effectively counsel their patients against smoking. Fortunately, most physicians already serve as nonsmoking role models for their patients.

TSUNG O. CHENG, MD
Professor of Medicine
Division of Cardiology
George Washington University
2150 Pennsylvania Ave, NW
Washington, DC 20037

REFERENCES

1. Pérez-Stable EJ, Fuentes-Afflick E. Role of clinicians in cigarette smoking prevention. West J Med 1998; 169:23–29

2. Epps, RP, Manley MW, Glynn TJ. Tobacco use among adolescents: strategies for prevention. Pediatr Clin North Am 1995; 42:389–402

Drs Pérez-Stable and Fuentes-Afflick Respond

To the Editor: Dr Cheng makes the important point that the personal example given by physicians in not smoking has been an important contributor in the decline in smoking rates in developed countries. Physicians in the United Kingdom were the first to stop smoking in large numbers, and this pattern has been followed by physicians in North America. We completely endorse the sixth "A" of abstaining from tobacco use and assume that the overwhelming majority of pediatric clinicians do not currently smoke.

Entering medical students in the United States smoke at a rate of about 1%, which is substantially lower than the prevalence of about 10% of physicians in the United States.[1] Thus, over the next 20 years, we should assume that the rate of smoking among physicians will continue to plummet, even though we have encountered increasing difficulties in impacting population smoking rates. We also note that up to 35% of physicians living in Latin America and Asia are current smokers of cigarettes, and this practice may impact immigrants coming from those countries.[2]

We do think the point made by Dr Cheng is important and relevant.

ELISEO J. PÉREZ-STABLE, MD
Professor of Medicine

ELENA FUENTES-AFFLICK, MD
Assistant Professor of Pediatrics
University of California, San Francisco
School of Medicine
400 Parnassus Avenue, A-405
San Francisco, California 94143-0320

REFERENCES

1. US Department of Health and Human Services. Tobacco and the Clinician: Interventions for Medical and Dental Practice. Washington, DC, US Department of Health and Human Services, Public Health Service, National Institutes of Health, NIH Publication No. 94-3693, 1994

2. US Department of Health and Human Services. Smoking and Health in the Americas. Atlanta, Georgia. US Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Center for Chronic Disease Prevention and Health Promotion, DHHS Publication No. (CDC) 92-8419, 1992

Poetry

* * *

Mnemonic

Jumbled anatomy lab box: sticks, knots
Ivory polished by years of touch
Fingered, fitted, laid in rows, decades
from the proper rest of graves.

Carpal, tarsal, incus, stapes,
Ilium, ischium, rib.
Conjure-names for destiny,
Spells with a terrible grace.

Grandma said her friend didn't have a single mean bone,
So for years I thought of one small bone, a spiky knot
Of meanness caught in certain people, maybe in the throat,
Making rattled ugliness whenever they talked.

Never Lower Tillie's Pants
Grandma Could Come Home
Navicular, lunate, triquetrium, pisiform
Scaphoid, capitate, cuboid, hamate.

Grandma got to be the scaphoid;
necessary bone, essential
for the proper use of hands:
knit, stir, spank, hug.

Wire-strung, castanet Mr. Bones
in the corner dressed for Halloween
Groucho glasses and cigar
Say the secret woid, Mr. Bones.

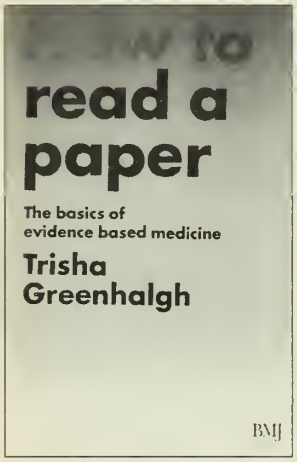
The ankle bone's connected to the knee bone
Fibula, tibia, femoral condyle
Dry bones have no remorse —
Always the last stone along the path.

Sinew-strung blocks, rag-tag scraps,
flesh a banner too-long flown
tattered by the years hanging from a staff.
Bones grow stronger under strain.

Until the day they snap and life rains down,
sculptured beauty splinters into pain.
Meanness is a given, soaks to the bone
but beauty doesn't stop at the skin.

Catharine Clark-Sayles
Mill Valley, California

Evidence based medicine...



How to Read a Paper

The Basics of Evidence Based Medicine

Trisha Greenhalgh

University College London, UK

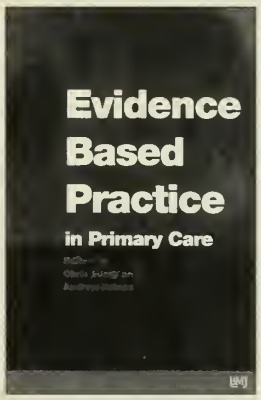
Written in a lively, jargon free style this best-selling book introduces the uninitiated reader to the principles of evidence based medicine and examines the criticisms levelled against it. The book covers such topics as literature searching, randomised controlled trials, and statistics for the non-statistician.

'An excellent book; it will reward those who study and apply its messages ...it transmits the author's personality, enthusiasm, and sense of humour.' *David L Sackett*

'This clear and concise book provides an excellent starting point for those interested in finding their way through medical literature.' *Palliative Medicine*

$26.95

0 7279 1139 2 PB 216 x 138 mm 184 pp. 1997 (Login Book # H2426)



Evidence Based Practice in Primary Care

Edited by *Christopher Silagy*

Flinders University of South Australia

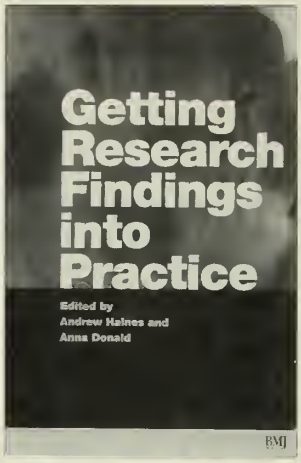
and *Andrew Haines*

Royal Free Hospital School of Medicine, London, UK

This guide is an introduction to those working in primary health care who have little or no knowledge of the theory and practice of evidence based medicine. The first section looks at the practicalities of applying EBM and its effect on decision making. The second section deals with the broader implications of EBM and how it affects professional practice internationally.

$45.00

0 7279 1210 0 PB 234 x 156 mm 208 pp. 1998 (Login Book # E0763)



Getting Research Findings into Practice

Edited by *Andrew Haines*

Royal Free Hospital School of Medicine, London, UK

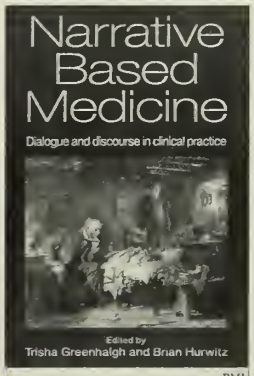
and *Anna Donald*

University College London, UK

Why is there such a wide gap betwe research findings and what actua happens in clinical practic This accessible guide provides practi suggestions for implementing eviden based medicine in health care. Drawi together the key issues, with seminal chapters from leading thinkers, includir criteria for implementation; evidence based practice for providers; hea economics; decision analysis; and closing the gap between research and practi

$35.95

0 7279 1257 7 PB 216 x 138 mm 180 pp. 1998 (Login Book # H3221)



Narrative Based Medicine

Dialogue and Discourse in Clinical Practice

Edited by *Trisha Greenhalgh*

University College London, UK

and *Brian Hurwitz*

Imperial College School of Medicine, London, UK

The central theme of this book is the narrati nature of illness and the consequent need f interpretation as well as investigation of t patient's problem.

'A timely book, and one which is both stimulating and controversial. It w provide a fascinating read for many people. I defy anyone who reads 'Th Conker Tree', or the patient based view of epilepsy, not to learn something.' *Kenneth Calman*

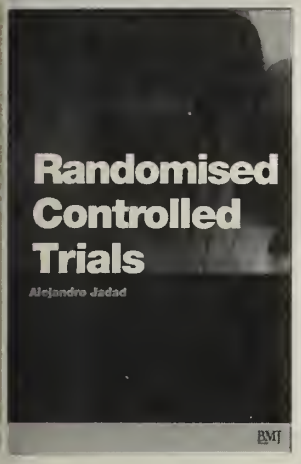
$35.95

0 7279 1223 2 PB 216 x 138 mm 304 pp. 1998 (Login Book # G3323)

BMJ Books are available from:

Login Brothers Book Company: Call: 888-858-7055 Fax: 800-339-1077 www.lb.com/bmj
1436 Randolph, Chicago, IL 60607 (Attn: Astralia/Donna) **and all good medical bookstores**

....from BMJ Books



Randomised Controlled Trials

Alejandro R Jadad
McMaster University, Canada

Written for anyone needing to understand RCTs, this readable handbook uses a question and answer format to explain all the basic information. Authored by an internationally known researcher from McMaster University, it provides a balanced view of the strengths and limitations of RCTs.

Contents include: RCTs: The basics; Types of RCTs; Assessing the quality of RCTs; Bias in RCTs; Reporting and interpreting individual trials; From trials to decisions: The basis of evidence based health care.

$23.50

0 7279 1208 9 PB 216 x 138 mm 128 pp. 1998 (Login Book # R2528)

Systematic Reviews

Edited by *Iain Chalmers*
Cochrane Centre, Oxford, UK
and *Douglas Altman*
Medical Statistics Laboratory, Imperial Cancer Research Fund, London, UK

A concise, ground-breaking book showing health care workers how to prepare a good review article and how to evaluate one.

'Attractively presented, highly readable, and packed with useful information.' *Journal of Clinical Nursing*

$26.95

0 7279 0904 5 PB 216 x 138 mm 128 pp. 1995 (Login Book # C14B3)

The Pocket Guide to Critical Appraisal

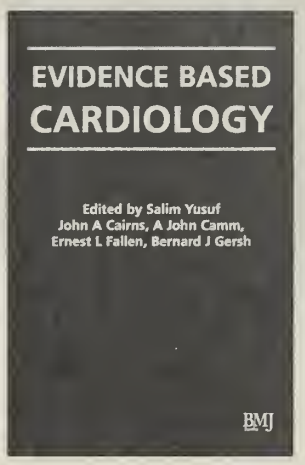
Iain K Crombie
Ninewells Hospital and Medical School, Dundee, UK

Everything you need to know to assess medical research is contained in this practical, accessible handbook. It provides a basic introduction to the principles and processes involved in critical appraisal, helping the researcher to make sense of the overwhelming mass of medical literature available.

'. a brief well-written and entirely helpful guide.' *Family Practice*

$19.95

0 7279 1099 X PB 216 x 138 mm 80 pp. 1996 (Login Book # C2514)



Evidence Based Cardiology

Edited by *Salim Yusuf*
McMaster University, Ontario, Canada
John Cairns, University of British Columbia, Vancouver, Canada
John Camm, St George's Hospital Medical School, London, UK
Ernest Fallen, McMaster University, Ontario, Canada and
Bernard Gersh
Georgetown University Medical Center, Washington, USA

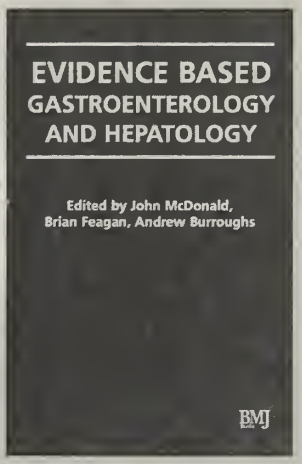
A ground-breaking text of major importance, addressing the implementation of evidence based medicine in the major cardiological subspecialties.

'Every physician and cardiologist should have a copy as a guide to the best treatment options for heart patients. Probably the most important publication in cardiological practice.' *Irish Medical Times*

$234.00

0 7279 1171 6 HB 260 x 190 mm 1200 pp. 1998 (Login Book # Y02B9)

From April 1999 a free electronic update to the text will be available at www.evidbasedcardiol.com



Evidence Based Gastroenterology and Hepatology

Edited by *John McDonald* and *Brian Feagan*
London, Ontario, Canada
and *Andrew Burroughs*
Royal Free Hospital, London, UK

Edited by leading gastroenterologists working in evidence based medicine, this text recommends best practice for treating the individual patient based on the randomised controlled trials and systematic reviews conducted in the major gastrointestinal and hepatobiliary subspecialties.

$117.00

0 7279 1182 1 HB 260 x 190 mm c.600 pp. July 1999
Introductory price until end of December 1999. (Login Book # M7201)

BMJ Books

Classified Advertisements

The rate for each insertion is **$1.50 per word, with a 30 word ($45) minimum.** Confidential box number charge: $10 each month.

A word is defined as one or more letters bounded by spaces. The following gives some examples:

Michael S. Wilkes, MD	= 4 words	allergy/immunology	= 1 word
Send CV	= 2 words	Sacramento, CA 95817	= 3 words
A	= 1 word	804-979-8034	= 1 word
February 22, 1997	= 3 words		

Classified display rate $70 per inch. Maximum sizes: 1 column by 5" or 2 columns by 2" (2-1/8" per column). Larger classified ad space by special arrangements.

Copy for classified advertisements should be received not later than **first of the month preceding issue. All copy must be typed or printed.** Classified advertisers using Box Numbers forbid the disclosure of their identity; your inquiries in writing will be forwarded to Box Number advertisers. Although *The Western Journal of Medicine* believes the classified advertisements in these columns to be from reputable sources, we do not investigate the offers made and assume no liability concerning them. The right is reserved to reject, withdraw, or modify all classified advertising copy in conformity with the decisions of the Advertising Committee.

Please Type or Print Advertising Copy

Classified Advertisements Are Payable in Advance

CLASSIFIED ADVERTISEMENTS, THE WESTERN JOURNAL OF MEDICINE
P.O. BOX 7690, SAN FRANCISCO, CA 94120-7690
(415) 974-1071; FAX (415) 882-3379
Ads may be placed online at www.wjmed.com

GET IN THE SWIM

PHOTO PARADE / EDDIE ADAMS

If you know a child with muscular dystrophy who can benefit from a special getaway, tell him or her about MDA summer camps. They're fun and free!

MDA Muscular Dystrophy Association
1-800-572-1717 • www.mdausa.org

PHYSICIANS WANTED

Physicians, B/E, FP, OB/GYN, IM, PED. Excellent salary, local and nationwide positions & hospital job orders. Fax CVs to 323-669-0270 or email CVs and orders to cloudy@ips.net. Medical Job Recruiters.

Coastal Oregon. Situated 75 miles west of Portland, Tillamook offers an excellent opportunity for a BC/BE Ob/Gyn. Family-oriented rural community with abundant outdoor recreational activities. Females encouraged to apply. Call Ingrid Heil at 800-847-9840 or fax curriculum vitae to 916-783-9909.

California, Northern–Internist needed for 70+ physician group affiliated with Catholic Healthcare West. Hospital and office-based practice (50/50) with shared call, competitive income and comprehensive benefits. Contact Danise Cooper, 800-765-3055; ID#: 6400 WE; fax 314-726-3009; email: dcooper@cejka.com. Visit our website at www.cejka.com.

California Coastal Community. Mid-size multispecialty group has opening for BC-BE Internal Medicine and Family Practitioners. Ventura is located 65 miles north of Los Angeles, has excellent schools, sunny beaches, friendly atmosphere, and a wide range of cultural/recreational activities. Attractive compensation and benefit package. Contact Physician Recruitment: Buenaventura Medical Group, 2705 Loma Vista Rd., Ventura, CA 93003. Phone 805-652-5240 or fax CV to 805-652 5299.

EQUIPMENT FOR SALE

FOR SALE: BONE DENSITY EQUIPMENT (HOLOGIC 1000 PLUS). Pencil Beam, 4-years old, excellent condition. Central Dexa (Hip and Spine) and Periph (forearm). Best offer. Call 505-522-2626, ask for Jean.

MEETINGS/CONFERENCES

The 10th International Symposium on Congenital Heart Disease in the Adult. June 3-5, 1999, Toronto, Ontario, Canada. Sponsored by American College of Cardiology. Program Co-directors: Peter P. Liu, MD, FRCP (C), FACC, and David J. Sahn, MD, FACC. 22 Category 1 credit hours. For information call 800-253-4636, ext. 695; fax 301-897-9745.

WESTERN STATES OPENINGS

Many multispecialty groups and hospitals have asked us to recruit for over 100 positions of various specialties. Both permanent and locum tenens. Send CV to:

Western States Physician Services
7510 No. Trellis Circle, Fresno, CA 93720
Call (800) 873-0786; FAX (800) 705-7943
email: weserve@lightspeed.net

California Department of Corrections

Health Care Services Division

HEALTH CARE MANAGER
CHIEF MEDICAL OFFICER

The California Department of Corrections has practice opportunities for BC/BE CA Licensed Physicians at various correctional facilities. You will be responsible for the management and quality assurance of the Medical Program; Pharmacy; Medical Records; Mental Health and Dentistry. Must be licensed to practice in California. Current opportunities exist at:

- California State Prison, Sacramento
- California State Prison, Corcoran
- High Desert State Prison, Susanville
- California State Prison, Corcoran
- Wasco State Prison Reception Center, Wasco

You will enjoy outstanding State of California Civil Service Benefits, with 13 paid holidays, health/dental/vision plans, generous vacation plan, professional liability coverage, safety retirement and much more.

To apply, contact Medical Recruiter, Health Care Services Division, P.O.Box 942883, Sacramento, CA 94283-0001. Phone: (916) 327-7081 or toll free (888) 232-4584, Fax: (916) 327-1436. Online: www.spb.ca.gov. EOE

HEALTH CARE SERVICES DIVISION
CALIFORNIA DEPARTMENT OF CORRECTIONS
PUBLIC SAFETY PUBLIC SERVICE

2/99

Defining the future of healthcare

Take a closer look at the future of healthcare, a future taking shape at The Cleveland Clinic Foundation. We have built the region's largest and most prestigious healthcare organization through a commitment to international leadership and top quality patient care, education and research.

The recent partnership between The Cleveland Clinic and the Wooster Clinic has created excellent opportunities for Board Certified/Eligible:

Internists • Cardiologists
Pulmonologists • Gastroenterologists

Enjoy the advantages of practicing personalized, community-based medicine combined with access to state-of-the-art facilities at The Cleveland Clinic's main campus. The Wooster, Ohio location offers a wonderful, family-oriented community, in a progressive college town. Become part of an expanding, multispecialty medical group.

Qualified professionals will receive a competitive salary, excellent benefits and paid meeting and vacation time. Send curriculum vitae to: **Attn: John Ferkan, Manager, Physician Recruitment, The Cleveland Clinic Foundation, P.O. Box #606140, Cleveland, OH 44106. Fax: 216-738-4059. email: ferkanj@cesmtp.ccf.org.** We are proud to be an equal opportunity employer. Smoke/drug-free environment.

Visit our homepage on the world wide web: **www.ccf.org**.

THE CLEVELAND CLINIC
Every Life Deserves World Class Care

The Western Journal of Medicine

Relaunch May 1999 –

A New Look for a New Millennium

The Western Journal of Medicine is to be relaunched in May 1999, following its recent purchase by UCSF Stanford Health Care in partnership with the British Medical Journal Publishing Group.

With a new look, new editors and many exciting new features, the relaunched journal is set to become a leading international medical publication, embracing the innovation of West Coast health care but with a broader, more international perspective.

The Western Journal of Medicine will also provide a stimulating and enjoyable read with regular debates on today's key health care issues and with a special emphasis on primary care.

For editorial and general queries, contact the WJM office in San Francisco.
Tel: 415-974 5977, **Fax:** 415-882 3379,
Email: wjmsf@pacbell.net

The Western Journal of Medicine

Publication: Monthly ISSN: 0093-0415
1999 Subscription rates:
Regular rate $70 US/Canada; $85 Rest of World
Institutional rate $120 US/Canada; $130 Rest of World
Student/Intern/Resident rate $20 US/Canada; $30 Rest of World

To order your subscription or a free sample copy, contact
BMJ Publishing Group, Box 590A, Kennebunkport ME 04046, USA;
Tel: 1-800-2-FON-BMJ; **Fax:** 1-800-2-FAX-BMJ
Email: bjpaige@cybertours.com

Flight of The Eagles(tm

Skytacular Destinations for Aviators

Ocean Cruise Conference '99

on

Aerospace Medicine

May 8 - 13, 1999

** Five (5) nights of luxury cruising on the Sun Princess.
** Meals and entertainment on board.
** Tour of the Boeing Factory at Everett.
** Tour of the Museum of Flight in Seattle.
** 15 hours of forums presented by leading AMEs on such vital topics as:

The Internet - Aeromedical Resources
The Enigma of Vertigo
Aerosinusitis, the Crew Menace Monster
Hypoxia and Decompression Sickness
Diseases Threatening Air Crew Certification
and more!

Call for a complete itinerary and list of topics.
From $895.00 per person. Spouse and child fares available.

Flight of the Eagles™ • Flight of the Eagles™ • Flight of the Eagles™

Flight of the Eagles™

Call: 714-957-2896 or
800-606-1626
Fax: 714-957-6829
Email: mindy@aeroglobe.com

Producer: Spirit of Flight Corporation
Email: gcurtis@loop.com
Web site: www.Eagles-Airlift.com

Western Journal of Medicine

INSTRUCTIONS FOR AUTHORS

In accordance with the Uniform Requirements for Manuscripts Submitted to Biomedical Journals (URM), 1997

Our readers represent all branches of medicine. We aim to publish manuscripts that are reliable and lively and that will improve the care of patients, the health of the public, or policies affecting either. Manuscripts should be of interest to a broad range of busy practitioners, physicians in training, and anyone who has an interest in health care. The purpose of a paper or letter may be to report, inform, alert, review, and discuss, but, above all, to teach. We aim to give quick and informative decisions on the articles we receive.

Manuscript Information

Manuscripts should be sent to the Managing Editor, Catherine Nancarrow, The Western Journal of Medicine, 221 Main Street, PO Box 7690, San Francisco, CA 94120-7690. Manuscripts must be original, not previously published, and not under consideration by another publisher. If preliminary data were included in another presentation or publication, this should be noted in the cover letter, and a copy of that publication should be included. Any conflict of interest, actual or potential, should be revealed to the Editors (see Letter of Transmittal). Obtaining informed consent to protect patients' rights to privacy should be documented according to URM 1997.

All manuscripts should be double-spaced and, including references and abstract but not tables, should not exceed:

- Original articles: 2,500 words with a maximum of five tables and 30 references
- Reviews: 1,500 to 2,000 words with a maximum of 25 references
- Topics in Primary Care Medicine: 2,000 words
- Evidence-Based Case Reports: 2,500 words with two tables and/or figures
- Commentaries: 600–800 words
- Letters to the Editor: 500 words

Manuscripts, except for Evidence-Based Case Reports, should include a structured abstract of no more than 250 words with the headings: objectives, design, setting, subjects, interventions, main outcome measures, results and conclusions.

Letters to the Editor must be double-spaced and will be published at the discretion of the Editors. They may be edited for style and brevity. Those of a scientific nature may be subject to peer review. They should be no more than 500 words in length.

All manuscripts will be subject to peer review in addition to review by the Editors to determine the originality, validity, and importance of content and conclusions. The WJM aims to introduce an open peer review system and reviewers' comments may be signed. Reviewers will be required to state possible conflicts of interest.

All accepted manuscripts are subject to copyediting, and the corresponding author is sent edited page proofs for approval and minor changes. It is the corresponding author's responsibility to clear all corrections and changes with coauthors.

Letter of Transmittal

All authors must sign the letter of transmittal, with one author designated as correspondent and his or her name, address, and telephone and fax numbers included.

The authors determine the order of authorship. All authors should meet the basic criteria for authorship (as stated below). Because the order of authorship is assigned in different ways, its meaning cannot be inferred accurately, unless it is stated by the authors. Authors may explain the order of authorship in a footnote.

A letter of transmittal, except for one accompanying a manuscript from US government employees whose work was done as part of their official duties, must include a paragraph that transfers copyright: "In consideration for reviewing and editing my submission, the author(s) undersigned hereby transfers, assigns, or otherwise conveys all copyright ownership to The Western Journal of Medicine, in the event that such work is published by the journal."

The letter of transmittal must include a statement of author responsibility signed by all authors: "I have participated in the conception and design of this work and in the writing of the manuscript and take public responsibility for it. I have reviewed the final version of the manuscript and approve it for publication. I attest to the validity and legitimacy of data in the manuscript and agree to be named as the lead author or coauthor of the manuscript."

The letter of transmittal must include a description of sources of funding and the role of sponsors, including their involvement, if any, in review and approval of the manuscript for publication. The letter must also include a statement of financial disclosure: "I warrant that I have no financial interest in the drugs, devices, or procedures described in the enclosed manuscript (except as disclosed in the attached statement)."

Research or project support should be included as a footnote to the manuscript or in the accompanying cover letter.

Manuscripts concerned with experimental investigation on human subjects must include in the text a statement that

all subjects gave their informed consent and that approval was obtained from the appropriate ethics committee.

Acknowledgments will be printed on a select basis to acknowledge those who contributed to but were not involved in the writing or review of the paper. They should not include persons whose work on the manuscript was a part of their regular duties.

Preparation of Manuscripts

Everything, including references, tables, figure legends, and abstracts, must be double-spaced.

Please submit the following: The original manuscript, two copies, and a copy of the manuscript on disk (formatted for a PC/Windows platform and labeled with the word processing program used). Allow a margin of 2.5 to 4 cm (1 to 1.5 in) on both sides. Be sure to include the references, tables, and figure legends on the disk. Formatting should be kept to a minimum. Manuscripts transmitted by facsimile machine are not acceptable unless requested by the Editors.

All values should be in Systeme International (SI) units, with metric equivalents following in parentheses. Temperature readings should be given in Celsius. Use the generic name of drugs, with the salt or ester given at the initial mention of a drug.

Figures should be submitted in triplicate in black and white, unmounted 12.7 × 17.8 cm (5 × 7 in) glossy prints, with the figure number, lead author's name, and top of the photo indicated with a label on the back.

The WJM encourages the use of illustrations and asks authors to submit photographs for publication. Patients should be asked to sign consent forms before pictures of them are published. This should be clearly stated and proof submitted with the manuscript. Changing the data on patients should not be used as a way of securing anonymity.

Figure legends, to be typed in sequence on the same page, should be in complete sentences. Any figures or tables previously published must be accompanied by a letter of permission to borrow from the copyright holder (the previous publisher). The permission of the authors should also be obtained. The Editors discourage the use of borrowed figures or tables.

Reprints

A form for ordering reprints will be sent to the corresponding author when the article is published.

References

All references should be cited in the text using superscript numbers and listed in their order of citation. The authors' names should be followed by the title of the article (abbreviated according to the style of Index Medicus), the year of publication, volume number, and first and last page numbers.

Journal Articles

Abbreviations of journal titles should conform to those used in Index Medicus. List up to three authors; for seven or more, use et al after listing the first three.

Vega KJ, Pina I, Krevsky B. Heart transplantation is associated with an increased risk for pancreatobiliary disease. Ann Intern Med 1996; 124:980–9832

Books

Author of book is same as author of chaper:

Ringsven MK, Bond D. Gerontology and Leadership Skills for Nurses. 2nd ed. Albany (NY). Delmar Publishers, 1996

Authors of book differ from chapter author:

Phillips SJ, Whisnant JP. Hypertension and stroke. In Laragh JH, Brenner BM (Eds). Hypertension: Pathophysiology, Diagnosis, and Management. 2nd ed. New York, Raven Press, 1995, pp 465–478

Correspondence

Shusterman D. Espresso maker's wrist [correspondence]. West J Med 1990; 152:721–722

Scientific or Technical Report

Issued by funding or sponsoring agency:

Smith P, Golladay K. Payment for durable medical equipment billed during skilled nursing facility stays. Final report. Dallas (TX): Dept of Health and Human Services (US), Office of Evaluation and Inspections; 1994 Oct. Report No.: HHSIGOEI69200860

Issued by performing agency:

Field MJ, Tranquada RE, Feasley JC, editors. Health services research: work force and educational issues. Washington DC: National Academy Press; 1995. Contract No.: AHCPR282942008

Sponsored by the Agency for Health Care Policy and Research. Centers for Disease Control and Prevention. Recommendations and Reports. 1997 Revised guidelines for performing $CD4^+$ T-cell determinations in persons infected with human immunodeficiency virus (HIV) MMWR Morb Mortal Wkly Rep 1997; 46(Jan 10):RR-2

Proceedings

Kimura J, Shibasaki H, editors. Recent advances in clinical neurophysiology. Proceedings of the 10th International Congress of EMG and Clinical Neurophysiology; 1995 Oct 15–19; Kyoto, Japan. Amsterdam: Elsevier; 1996

Mass Circulation Publications

Lee G. Hospitalizations tied to ozone pollution: study estimates 50,000 admissions annually. The Washington Post 1996 Jun 21; Sect A:3 (col 5)

Personal Communications and Unpublished Data

The use of "personal communication" or "unpublished data" should be avoided and should not be

included in the reference list. If such a notation provides essential information not available from a public source, it should be given in parentheses in the body of the text, listing the person's name, highest academic degrees, and professional affiliation, whether the communication was oral or written, and the date (month and year): Lyme disease has been reported in red squirrels (J. Sneed, PhD, Department of Wildlife, written communication, September 1990)

For Further Information

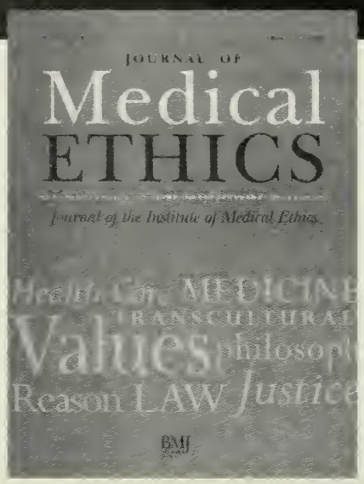
Questions regarding the Instructions for Authors may be directed to the Managing Editor in writing at the address above or by telephone (415) 974-5977, Fax (415) 882-3379.

AUTHOR CHECKLIST

- ✓ Original manuscript and two copies, as well as PC diskette.
- ✓ Everything double-spaced.
- ✓ Illustrations, black and white glossy, identified with lead author's name, plus figure legends that describe fully and in complete sentences what the figure depicts.
- ✓ Letter of transmittal that includes release of copyright, statement of conflict of interest, funding source(s), and authorship responsibility, signed by all the authors.
- ✓ A 250-word structured abstract.
- ✓ Title page that includes current affiliation of all authors and an address and telephone and fax number for corresponding author.
- ✓ Permission-to-borrow letters for any previously published illustrations or tables.
- ✓ Informed consent obtained.

Journal of Medical ETHICS

DOUBLE ISSUE - April '99



Announcing the April special issue...

Ethics and the new genetics

The April issue of the *Journal of Medical Ethics* will be a double issue of about 25 papers dedicated to the subject of ethics and the new genetics. The guest editors are Professor Bob Williamson and Associate Professor Julian Savulescu of the Murdoch Institute for Research into Birth Defects, Melbourne, Australia.

It will be of interest and benefit to a wide cross section of clinical and non-clinical professionals at a time of rapid and profound change in this area.

The issue comprises peer reviewed articles covering a wide range of issues: ethical problems raised by the prospect of human cloning, ethical and social issues around genetic screening and preimplantation genetic diagnosis, genetic testing in the wider arena of justice, and more.

Articles in this issue include:

- Should we clone human beings? Cloning as a source of tissue for transplantation
  Julian Savulescu and commentary by Bob Williamson
- Genetic screening with the DNA chip: a new Pandora's box?
  Wolfran Henn
- Beyond the disorder: one parent's reflection on genetic counselling
  Ruth Mc Gowan
- Preimplantation genetic diagnosis and the 'new' eugenics
  David King
- Does justice require genetic enhancement?
  Nils Holtung
- Genetic privacy: orthodoxy or oxymoron?
  Veronica English and Anne Sommerville

Individual copies are available to non-subscribers to the Journal of Medical Ethics from April '99. UK price £10 per copy including postage; overseas £12 per copy ($19 in the US) including postage.

Send orders to BMJ Publishing Group, PO Box 299, London WC1H 9TD, UK.
Tel +44 (0) 171 383 6270, Fax +44 (0) 171 383 6402, Email:subscriptions@bmjgroup.com.
Send US orders to: BMJ Publishing Group, Box 590A, Kennebunkport ME 04046, USA
Tel: 1-800-2-FON-BMJ Fax: 1-800-2-FAX-BMJ

BMJ Publishing Group

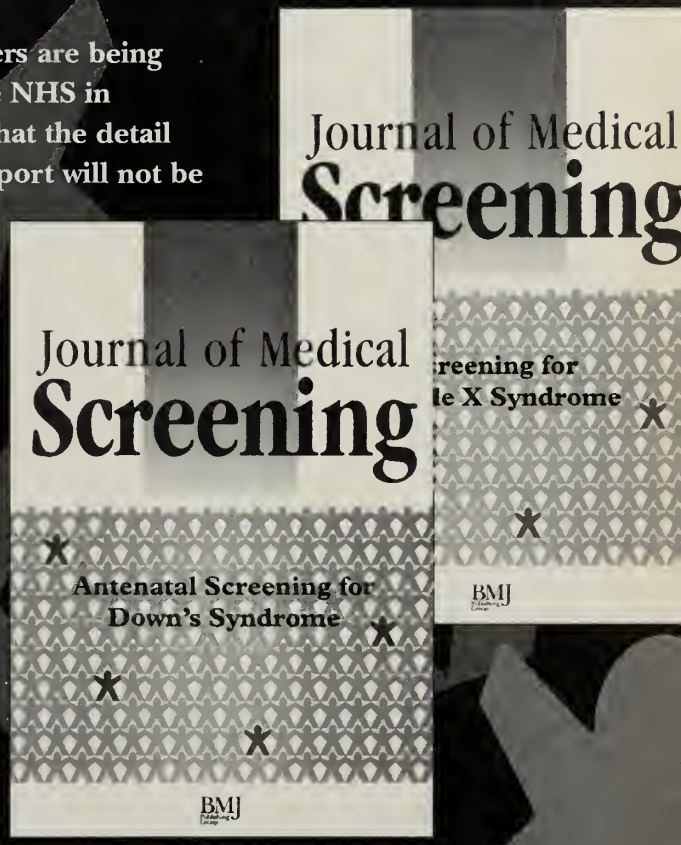
Systematic Reviews of
SCREENING

Systematic reviews of screening for various disorders are being commissioned by health authorities, including the NHS in Britain. They are generally not published in full, so that the detail and the full list of references used to produce the report will not be made available.

Now available from BMJ are two full reviews, *Screening for Fragile X Syndrome* and *Antenatal Screening for Down's Syndrome*, published as special issues of Journal of Medical Screening.

Screening for Fragile X Syndrome aims at providing the information needed by health planners to judge whether or not to use DNA testing to screen for the disorder.

Antenatal Screening for Down's syndrome provides what is probably the most comprehensive and up to date summary of the subject that will be valuable to anyone involved in screening or responsible for making decisions on screening.



ORDER FORM

PLEASE SEND ME
Journal of Medical Screening:

- ☐ **Screening for Fragile X Syndrome**
- ☐ **Antenatal Screening for Down's Syndrome**

Price: £12.50/$21 USA only

☐ I enclose a cheque for .....(Payable to BMJ)

Sterling cheques to be drawn on a UK bank account.
US Dollar cheques to be drawn on a US bank account.

☐ Charge my credit card £/$.....

☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐

American Express/Visa/Mastercard/Delta/Switch
(delete as appropriate)

Issue No .....(Switch Cards only)

Expiry date .....Signature.....
(Your signature is essential when paying by credit card)

If your billing address differs from below, please advise us

Name.....

Specialty/Position .....

Address.....

.....

Country .....Postcode.....

☐ Please tick if you do not wish your data to be used for direct marketing purposes

Send orders to: BMJ Publishing Group, Journals Marketing Dept., PO Box 299, London WC1H 9TD, UK. Fax credit card orders to +44 (0)171 383 6402 Call our subscription hotline on +44 (0)171 383 6270 or BMJ Publishing Group, Box S90 A, Kennebunkport, ME 04046 USA. Tel 1-800-2-FON-BMJ Fax 1-800-2-FAX-BMJ

INVITATION TO DELEGATES

SWEDISH HEALTH SERVICE QUALITY AWARD 1999

A Three Day Conference
Tuesday 25 - Thursday 27 May 1999
STOCKHOLM INTERNATIONAL FAIRS
SWEDEN

4th European Forum on Quality Improvement in Health Care and 4th Swedish QUL Conference

THEMES OF THE FORUM

- *Accelerating clinical improvement*
- *Quality improvement in primary care*
- *Making health better in the community*
- *Promoting evidence - based health care*
- *Building partnerships with patients*
- *Measurement for quality improvement in health care*
- *Leading change*
- *Increasing access and reducing delay in health care*
- *Harnessing information and communication technology for health improvement*
- *Putting quality improvement at the heart of education of health care professionals*

AIMS OF THE FORUM

- *To provide education on how to improve health care*
- *To exchange sound, practical ideas on improving health care*
- *To provide a setting for deep discussion and shared learning among those charged with leading improvements in health care*
- *To build the scientific base of methods to improve health care*

PRINCIPLES OF THE FORUM

- *Emphasis on what works*
- *Learning through experience*
- *Concentrating on improvement rather than inspection*
- *Patient orientation*
- *Multidisciplinary*
- *Basing change on measurement*
- *Team orientation*
- *Cost consciousness*
- *Encouraging efficiency*
- *All teach, all learn*

FOR FURTHER INFORMATION, PLEASE COMPLETE AND RETURN THE FORM BELOW.

INSTITUTE FOR HEALTHCARE IMPROVEMENT

Supported by

THE FEDERATION OF SWEDISH COUNTY COUNCILS

BMJ Publishing Group

Please send me further details on the 4th European Forum on Quality Improvement in Health Care and 4th Swedish QUL Conference.

Name: _____

Address: _____

_____

_____

Postcode: _____ Country: _____

Job/Position: _____

Telephone: _____ Fax: _____

E-mail: _____

Please return this form to Marchella Mitchell, BMA/BMJ Conference Unit, PO Box 295, London, WC1H 9TE.
Fax: +44 (0) 171 383 6869 Email: MMitchell@bma.org.uk

PUBLISHED BIMONTHLY

JOURNAL OF

Medical ETHICS

BMJ Publishing Group

Journal of the Institute of Medical Ethics

Editor: Raanan Gillon

First published in 1975, *Journal of Medical Ethics* is a leading international journal featuring interdisciplinary articles on ethical aspects of health care. With an increase in frequency from quarterly to bimonthly, the journal offers original articles, case conferences, editorials, book reviews, correspondence, news and notes.

A Selection of Recent Papers:

"Goodbye Dolly?" The ethics of human cloning
John Harris

At the coalface - medical ethics in practice: First, do no harm
Scott Groudine and Philip D Lumb

Patients' rights in England and the United States of America: The Patients's Charter and the New Jersey Patient Bill of Rights: a comparison
Melanie H Wilson Silver

Subscription Rates

Institutional: Worldwide £132, USA Only $214

Personal: Worldwide £90, USA Only $146

Student Rate: Worldwide £47, USA Only $76*

* (Please send proof of student status)

VISIT OUR HOMEPAGE ON: **www.jmedethics.com**

ORDER FORM

Journal of Medical Ethics

ISSN 0306 6800 Publication: Bimonthly
1999 Subscription Rate: Institutional: Worldwide £132, USA Only $214
Personal Rate: Worldwide £90, USA Only $146
Student Rate: Worldwide £47, USA Only $76*
***(Please send proof of student status)**

☐ Send me instructions to Authors

☐ Send me a free sample copy

☐ Enter my subscription, starting from: .....

☐ I enclose a cheque for £/$ .....
(Payable to BMJ)

☐ Charge my credit card £/$.....

☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐

American Express/Visa/Mastercard/Delta/Switch
(delete as appropriate)

Switch Issue Number .....

Expiry date .....Signature .....
(Your signature is essential when paying by credit card)
If your billing address differs from below, please advise us

Name.....

Address.....

.....

Postcode .....Country .....

N.B. Subscribers in the following countries must add tax to the quoted sterling price unless they can provide a registration number: Canada - 7% GST, Italy and Spain - 4% IVA, Ireland - 21%, Germany - 7% MWS, Belgium - 6% TVA/BTW and France - 20.6% TVA

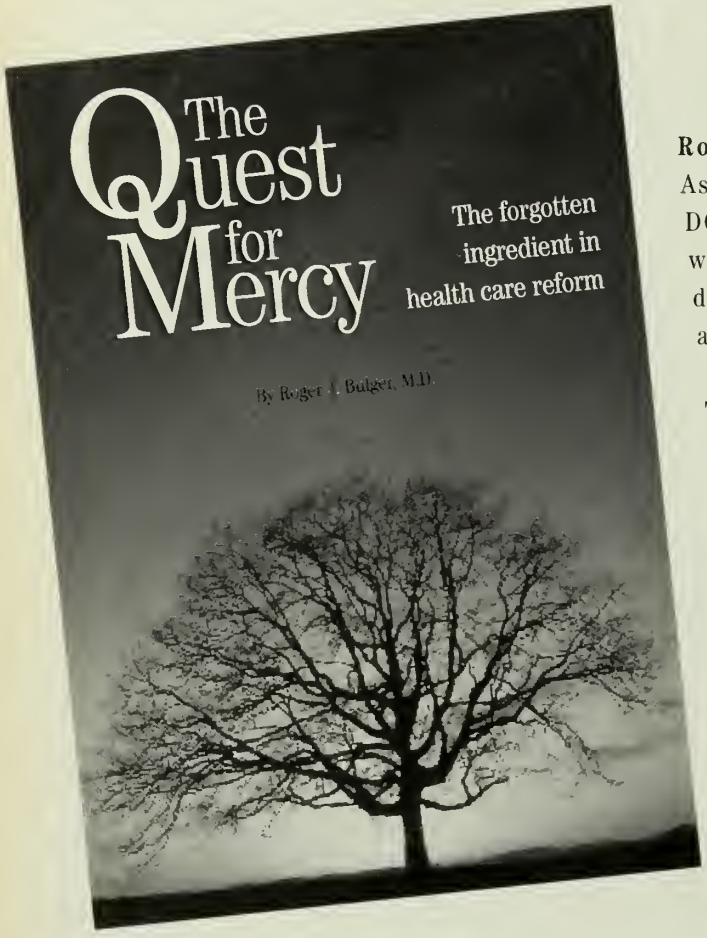
***Send orders to:* BMJ Publishing Group, Journals Marketing Dept., PO Box 299, London WC1H 9TD, UK.**

***Orders in the U.S:* BMJ Publishing Group, Box 509A, Kennebunkport, ME 04046, USA.**
Tel: 1-800-2-FON-BMJ Fax: 1-800-2-FAX-BMJ

The Quest for Mercy

The forgotten ingredient in health care reform

by Roger J. Bulger, MD, FACP



Roger J. Bulger, MD, FACP is President of the Association of Academic Health Centers in Washington, DC. He has published scores of papers and chapters, as well as three books on subjects ranging from infectious diseases to medical education, humanities, Hippocrates, and, of course, academic health centers.

The Quest for Mercy is aimed at physicians, including young physicians and medical students. The book addresses managed care and managed cost, sickness and healing, hope and despair, relationships, oaths, populations, prevention, and patients.

"This book will become a classic."

Linda Hawes Clever, MD
Editor, THE WESTERN JOURNAL OF MEDICINE

The Complete Manuscript As Published I
The Western Journal of Medicin

ORDER YOUR COPIES NOW!

Per Copy: $10.00*

*Note: USA/Canada postage and handling included, all other countries please add US $6.00 Air Printed Matter postage. Please add Virginia and local sales tax where applicable. Quantity discounts available; please call.

I would like to order_____copy(ies) of **The Quest For Mercy**.
Payment must accompany order. Total amount enclosed $_____

NAME _____

INSTITUTION _____

ADDRESS _____

CITY/STATE/ZIP _____

COUNTRY _____

❑ Check Enclosed $_____ *please charge my* ❑ VISA ❑ MASTERCARD
(*make payable to:* The Western Journal of Medicine)

Account #_____ Exp. date _____

Signature _____

CARDEN JENNINGS
PUBLISHING CO., LTD.

MAIL TO: *The Western Journal of Medicine*, 1224 West Main Street, Suite 200, Charlottesville, Virginia 22903-2858
Phone: (804) 979-8034 • Fax: (804) 979-4025 • www.wjmed.com

For reprints opportunities, please contact:

Sheila Williams (Quotations)
Tel: +44 (0)171 383 6305 Fax: +44 (0)171 383 6699
Email: swilliams@bmjgroup.com

Sheila Rowe (Sales Enquiries)
Tel: +44 (0)171 383 6450 Fax: +44 (0)171 383 6556
Email: jwheeler@bmjgroup.com

For enquiries within USA & Canada, please contact: Marsha Fogler
Tel: 1(800) 482 1450 or 1(609) 482 9665 Fax: 1(609) 482 7414
Email: fogler@erols.com

BMJ Bookshop

TITLES Extensive database of medical and related titles

INFORMATION Book information includes contents lists and descriptions

SEARCH User friendly searching by key word and subject category

ORDERING Flexible and secure online ordering options

BESTSELLERS Top 10 and new title features

bmjbookshop

The online bookshop for medical professionals –
open 24 hours a day

OFFICIAL JOURNAL OF

ARIZONA MEDICAL ASSOCIATION · CALIFORNIA MEDICAL ASSOCIATION · DENVER MEDICAL SOCIETY · IDAHO MEDICAL ASSOCIATION · NEVADA STATE MEDICAL ASSOCIATION · NEW MEXICO MEDICAL SOCIETY · UTAH MEDICAL ASSOCIATION · WASHINGTON STATE MEDICAL ASSOCIATION · WYOMING MEDICAL SOCIETY

The Western Journal of Medicine

VOLUME 170 • NUMBER 4 APRIL 1999

197 Letter From the Editors
MS WILKES AND M SHUCHMAN

ORIGINAL RESEARCH

198 Methamphetamine Abuse and Emergency Department Utilization
JR RICHARDS, SW BRETZ, EB JOHNSON, SD TURNIPSEED, BT BROFELDT, AND RW DERLET

203 Fracture Epidemiology and Control in a Developmental Center
G-S LOHIYA, FM CRINELLA, L TAN-FIGUEROA, S CAIRES, AND S LOHIYA

210 Type 2 Diabetes Mellitus in Navajo Adolescents
C KIM, C McHUGH, Y KWOK, AND A SMITH

ARTICLES

214 Methamphetamine and the Expanding Complications of Amphetamines
TE ALBERTSON, RW DERLET, AND BE VAN HOOZEN

220 Update on the Status of Africanized Honey Bees in the Western States
KT KIM AND J OGURO

223 Mass Envenomations by Honey Bees and Wasps
RS VETTER, PK VISSCHER, AND S CAMAZINE

228 Description of an Ethics Curriculum for a Medicine Residency Program
HJ SILVERMAN

EDITORIALS

232 The Problem of Methamphetamine Toxicity
S KARCH

233 The JAMA Firing
M SHUCHMAN

234 A Letter to the Executive Vice-President of the American Medical Association from Linda Hawes Clever
LH CLEVER

235 An "Old Timer" Reflects on the Use of the "Placebo Effect"
B COOPERMAN

COMMENTARIES

237 Ash Wednesday
RR PESCE

239 Resuscitating Annie
M DENNEY

240 Confessions of a Beggarly Doctor
R CRAWSHAW

CORRESPONDENCE

242 Death of a Truck Driver: Fatal Nicotinamide Poisoning Associated with Intravenous Drug Use
KB NOLTE, RB PALMER, AND NGS RAO

243 Biological Warfare
J SUCHARD

OTHER FEATURES

192 Continuing Medical Education Activities

244 Classified Advertising

245 Instructions for Authors

Detailed Table of Contents: 190 101

THE FRANCIS A. COUNTWAY LIBRARY OF MEDICINE BOSTON, MA
JAN 16 2001

RECEIVED
NOV 24 1999
ARMED FORCES MEDICAL LIBRARY

Affiliated Clinical Investigation Societies: the Western Association of Physicians; the Western Society for Clinical Investigation; the Western Section, American Federation for Medical Research; the Western Society for Pediatric Research; the Western Region, Society for Investigative Dermatology

Full text, free access.

– Fully searchable archive –

– 150 topic collections –

– Customised email alerting –

– Rapid responses –

– Enhanced articles –

– Extra news stories –

– Direct Medline access –

– Jobs, courses, and careers –

And we don't ask you to pay, subscribe, register, provide passwords, or fill in interminable online questionnaires.

www.bmj.com

THE FRANCIS A. COUNTWAY
LIBRARY OF MEDICINE
BOSTON, MA

The Western Journal of Medicine®

SINCE 1902

P.O. BOX 7690 • SAN FRANCISCO, CALIFORNIA 94120-7690
221 MAIN STREET • SAN FRANCISCO, CALIFORNIA 94105
TELEPHONE (415) 974-5977; FACSIMILE (415) 882-3379; E.MAIL wjmsf@pacbell.net

JAN 16 2001

MICHAEL S. WILKES, *Editor*
MIRIAM SHUCHMAN, *Editor*

CATHERINE NANCARROW, *Editorial Manager*
NEIL POPPMACHER, *Production Manager*
RUTH STAUNTON, *Business Manager*

editorial communications to CATHERINE NANCARROW • business communications to RUTH STAUNTON

Official Journal of the Alaska State Medical Association, the Arizona Medical Association, the California Medical Association, the Denver Medical Society, the Idaho Medical Association, the Nevada State Medical Association, the New Mexico Medical Society, the Utah Medical Association, the Washington State Medical Association, and the Wyoming Medical Society.

Affiliated Clinical Investigation Societies: the Western Association of Physicians; the Western Society for Clinical Investigation; the Western Section, American Federation for Medical Research; the Western Society for Pediatric Research; the Western Region, Society for Investigative Dermatology.

SPECIAL EDITORS

Special Editor for Arizona
Marshall B. Block, Phoenix, AZ

Special Editor for Denver
David Shander, Denver, CO

Special Editor for Idaho
E. R. W. Fox, Coeur d'Alene, ID

Special Editor for Nevada
Anton P. Sohn, Reno, NV

Special Editor for New Mexico
I. Brian Taylor, Carlsbad, NM

Special Editor for Utah
C. Basil Williams, Salt Lake City, UT

Special Editor for Washington
David Hopkins, Federal Way, WA

Special Editor for Wyoming
Joseph P. Murphy, Casper, WY

ASSISTANT EDITORS

Clinical Investigation
H. Benfer Kaltreider

Health and Public Policy
Ralph Crawshaw

International Health
Anvar Velji

Lessons From the Practice
Stephen J. McPhee
Jonathan E. Rodnick

Medical Staff Conferences
Nathan M. Bass

Poetry
Margaret Kaufman

Primary Care Medicine
Stephen J. McPhee
Terrie Mendelson

Radiologic Cases
Jonathan M. Levy

EDITORIAL BOARD

Editor Emeritus
Malcolm S. M. Watts, San Francisco, CA

Anesthesiology
Carol Lake, Sacramento, CA

Biostatistics and Epidemiology
Virginia L. Emster, San Francisco, CA

Cardiac and Thoracic Surgery
Norman E. Shumway, Stanford, CA

Dermatology
Clifton R. White Jr, Portland, OR

Emergency Medicine
William A. Boehm, Alamogordo, NM

General and Family Practice
Norman Kahn, Kansas City, MO
Thomas E. Norris, Seattle, WA
Joe Schoeber, Casper, WY

Internal Medicine
Albert Deisseroth, Houston, TX
Alan Fogleman, Los Angeles, CA
Patricia Gabow, Denver, CO
John H. Holbrook, Salt Lake City, UT
Philip Hopewell, San Francisco, CA
Irwin J. Schatz, Honolulu, HI
Walter E. Stamm, Seattle, WA
Reginald Strickland, Albuquerque, NM
Stephen I. Wasserman, San Diego, CA

Neurology
Robert Collins, Los Angeles, CA
John Greenlee, Salt Lake City, UT
Leslie Wiener, Los Angeles, CA
Earl Zimmerman, Portland, OR

Neurosurgery
George A. Ojemann, Seattle, WA
Robert F. Spetzler, Phoenix, AZ

Nuclear Medicine
Jerold M. Lowenstein, San Francisco, CA

Obstetrics and Gynecology
Daniel Mishell Jr, Los Angeles, CA

Occupational Medicine
Linda Rosenstock, Washington, DC

Ophthalmology
Sandy Feldman, La Jolla, CA

Orthopedics
Thomas DeCoster, Albuquerque, NM

Pathology
Ronald Weinstein, Tuczon, AZ

Pediatrics
Allen W. Mathies Jr, Pasadena, CA
Diane Wara, San Francisco, CA

Pharmacology
Rubin Bressler, Tucson, AZ

Physical Medicine and Rehabilitation
Julie G. Madorsky, Pomona, CA

Preventive Medicine and Public Health
Joseph L. Lyon, Salt Lake City, UT

Psychiatry
J. Christian Gillin, San Diego, CA
Lewis Judd, La Jolla, CA

Radiology
Gary Glazer, Stanford, CA
Michael L. Manco-Johnson, Denver, CO
Albert A. Moss, Seattle, WA

Surgery
Haile T. Debas, San Francisco, CA
Alex G. Little, Las Vegas, NV

Urology
Linda Shortliffe, Stanford, CA

Senior Members at Large
Thomas Elmendorf, Davis, CA
Edgar Waybum, San Francisco, CA

ADVISORY BOARD, CLINICAL INVESTIGATION

Brian A. Cason, San Francisco, CA
John Christenson, Salt Lake City, UT
Kari Connolly, San Francisco, CA
Bruce W. Goldberg, Portland, OR
Philip Goodman, Reno, NV
Roy Jones, Albuquerque, NM
Howard Lien, Tucson, AZ
Barbara M. Lippe, Los Angeles, CA
Michael W. McDermott, San Francisco, CA
Jeanette Mladenovic, Denver, CO
Kenneth M. Moser, San Diego, CA
James C. Orcutt, Seattle, WA
John Owings, Sacramento, CA
Robert Robbins, Stanford, CA
Henry Rosen, Seattle, WA
Mary H. Samuels, Portland, OR
George A. Sarosi, San Jose, CA
Jeffrey Saver, Los Angeles, CA
David Schriger, Los Angeles, CA
Jack H. Simon, Denver, CO
Peggy Sue Weintrub, San Francisco, CA
Owen M. Wolkowitz, San Francisco, CA

DISPLAY ADVERTISING INFORMATION

CONTACT: Alan Walker, BMJ Publishing Group, BMA House, Tavistock Square, London WC1H 9JR, UK • (+44) 171-383-6226/FAX (+44) 171-383-6556. Email: awalker@bmj.com

Advertisements—The journal is published the second week of the month. Display advertising must be received no later than the first of the month preceding issue. Advertising rates will be sent on request. Acceptance of advertising is contingent upon approval by the Publisher.

The journal reserves the right to reject any advertisement.

CLASSIFIED ADVERTISING

CONTACT: Ruth Staunton, The Western Journal of Medicine, P.O. Box 7690, San Francisco, CA 94120-7690 • (415) 882-5177/FAX (415) 882-3379.

SUBSCRIPTION INFORMATION

The subscription price is $70 per year and $130 for 2 years in the United States and Canada (US funds); $85/$160 in all other countries. Institutional rate in the United States is $120/$240; $130/$260 all other countries. Single copies are $15. Address all subscription communications to:

WJM, P.O. Box 590A, Kennebunkport, ME 04046 • 800-236-6265 • 800-232-9265.
E-mail: bjpaige@cybertours.com

Allow six weeks for subscriptions to begin. Past issues must be bought individually. So long as reserve stocks are available, missing issue requests from subscribers are honored for up to six months after the issue date. Thereafter, the single copy rate of $15 is applicable for each issue available.

Change of Address—Requests for change of address should give both the old and new address. Allow six weeks for changeover.

SUBMITTING MANUSCRIPTS

Manuscripts for consideration should be sent to the editorial manager, C. Nancarrow, The Western Journal of Medicine, P.O. Box 7690, San Francisco, CA 94120-7690.

"Guidelines for Authors"—A complete guide to manuscript submission and *WJM* style available from the publisher. Manuscripts may be prepared in accordance with the "Uniform Requirements for Manuscripts Submitted to Biomedical Journals."

PUBLISHER

Copyright © 1999 by the British Medical Journal Publishing Group • Owned and Published by BMJ Publishing Group and UCSF Stanford Healthcare
All material subject to this copyright appearing in THE WESTERN JOURNAL OF MEDICINE may be photocopied for the noncommercial purpose of scientific or educational advancement. Volumes begin with January and July.

THE WESTERN JOURNAL OF MEDICINE (ISSN 0093-0415/USPS 084 480) is published monthly by BMJ Publishing Inc, 221 Main St., San Francisco, CA 94105. Mail correspondence to WJM–BMJ Publishing Inc., P.O. Box 7690, San Francisco, CA 94120-7690. Periodicals postage paid at Easton, Pennsylvania.
POSTMASTER: Send address changes to *The Western Journal of Medicine*, P.O. Box 7690, San Francisco, CA 94120-7690.

The Western Journal of Medicine

VOLUME 170 • NUMBER 4 • APRIL 1999

CONTENTS

197 **Letter From the Editors**

MICHAEL S. WILKES, MD, PHD, and MIRIAM SHUCHMAN, MD

ORIGINAL RESEARCH

198 **Methamphetamine Abuse and Emergency Department Utilization**

JOHN R. RICHARDS, MD; STEPHEN W. BRETZ, MD; EMILY B. JOHNSON; SAMUEL D. TURNIPSEED, MD; B. TOMAS BROFELDT, MD; and ROBERT W. DERLET, MD

From the Division of Emergency Medicine, University of California, Davis Medical Center, Sacramento, California.

203 **Fracture Epidemiology and Control in a Developmental Center**

GHAN-SHYAM LOHIYA MD, MS; FRANCIS M. CRINELLA PHD; LILIA TAN-FIGUEROA, MD; SHIRLEY CAIRES PHN, CIC; and SONIA LOHIYA

From the Fairview Developmental Center, Costa Mesa, California; the Department of Pediatrics, University of California, Irvine, California; and the Eleventh Grade, Corona Del Mar High School, Newport Beach, California.

210 **Type 2 Diabetes Mellitus in Navajo Adolescents**

CATHERINE KIM, MD, MPH; CHRISTINA McHUGH, MD; YEONG KWOK, MD; and APRIL SMITH, RD, CDE, MPH

From the United States Public Health Service, Crownpoint Healthcare Facility, Crownpoint, New Mexico.

ARTICLES

214 **Methamphetamine and the Expanding Complications of Amphetamines**

TIMOTHY E. ALBERTSON, MD, PHD; ROBERT W. DERLET, MD; and BRENT E. VAN HOOZEN, MD

From the Division of Pulmonary and Critical Care Medicine, University of California, Davis, Medical Center, Sacramento, California; Division of Emergency Medicine and Clinical Toxicology, Section of Pulmonary Medicine, Veterans Administration Northern California Health Care System Mather, Sacramento, California; and Sacramento Division, California Poison Control Center, Sacramento, California.

220 **Update on the Status of Africanized Honey Bees in the Western States**

KENNETH T. KIM, MD, and JODI OGURO

From the Allergy, Asthma, and Respiratory Care Center, Inc, Long Beach, California; and the undergraduate program at the University of California, Berkeley, California.

223 **Mass Envenomations by Honey Bees and Wasps**

RICHARD S. VETTER, MS; P. KIRK VISSCHER, PHD; and SCOTT CAMAZINE, MD, PHD

From the Department of Entomology, University of California, Riverside, Riverside, California; and the Department of Entomology, Penn State University, University Park, Pennsylvania.

228 **Description of an Ethics Curriculum for a Medicine Residency Program**

HENRY J. SILVERMAN, MD, MA

From the Department of Medicine, University of Maryland School of Medicine, Baltimore, Maryland.

EDITORIALS

232 **The Problem of Methamphetamine Toxicity**

STEVEN KARCH, MD

Assistant Medical Examiner, City and County of San Francisco, San Francisco, California

233 **The JAMA Firing**
MIRIAM SHUCHMAN, MD
From The Western Journal of Medicine.

234 **A Letter to the Executive Vice-President of the American Medical Association from Linda Hawes Clever**
LINDA HAWES CLEVER, MD, MACP
From the Department of Occupational Health, California Pacific Medical Center.

235 **An "Old Timer" Reflects on the Use of the "Placebo Effect"**
BERNARD COOPERMAN, MD
From the Alban-Wertheimer Orthopaedic Group, Los Alamito, California.

COMMENTARIES

237 **Ash Wednesday**
RICHARD R. PESCE, MD
From the Chattanooga Heart Institute, Chattanooga, Tennessee.

239 **Resuscitating Annie**
MIKE DENNEY, MD, FACS
In private practice in Sausalito, California.

240 **Confessions of a Beggarly Doctor**
RALPH CRAWSHAW, MD
In private practice in Portland, Oregon.

CORRESPONDENCE

242 **Death of a Truck Driver: Fatal Nicotinamide Poisoning Associated with Intravenous Drug Use**
KURT B. NOLTE, MD; ROBERT B. PALMER, PHD; and N. G. S. RAO, PHD
From the Office of the Medical Investigator, University of New Mexico School of Medicine, Albuquerque, New Mexico; Medical Examiner/Coroner Information Sharing Program, National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, Georgia; Toxicology Program, College of Pharmacy, University of New Mexico, Albuquerque, New Mexico; State of New Mexico, Scientific Laboratory Division, Toxicology Bureau, Albuquerque, New Mexico.

243 **Biological Warfare**
JEFFREY SUCHARD, MD
Department of Medical Toxicology, Good Samaritan Regional Medical, Phoenix, Arizona.

OTHER FEATURES

192 **Continuing Medical Education Activities**

244 **Classified Advertising**

245 **Instructions for Authors**

★ Official Journal of the Alaska State Medical Association, the Arizona Medical Association, the California Medical Association, the Denver Medical Society, the Idaho Medical Association, the Nevada State Medical Association, the New Mexico Medical Society, the Utah Medical Association, the Washington State Medical Association, and the Wyoming Medical Society.

Continuing Medical Education

ARIZONA • CALIFORNIA, HAWAII, NEVADA • COLORADO • IDAHO • NEW MEXICO • UTAH • WASHINGTON • WYOMING

ARIZONA

All courses listed have been certified as meeting the criteria for Category I of the ArMA CME Certificate and the AMA Physicians Recognition Award. To list Category I CME programs, please send information to Arizona Medical Association, 810 West Bethany Home Road, Phoenix, AZ 85013; or phone (602) 246-8901.

Brochures and registration forms are available from the contact person or organization sponsoring the program.

October 29–31, 1999—**Neurology for the Non-Neurologist.** The Phoenician, Scottsdale, AZ. CME 11 hrs Category 1. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; (800) 421-3756; Fax (303)798-5731.

December 10–12, 1999—**Managing Respiratory Disease.** The Phoenician, Scottsdale, AZ. CME 11 hrs Category 1. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; (800) 421-3756; Fax (303)798-5731.

CONTACT INFORMATION

Mayo Clinic-Scottsdale—Contact: Postgraduate Courses, Mayo Clinic-Scottsdale, (602) 301-7447.

U of A—Contact: University of Arizona College of Medicine, Arizona Health Sciences Center, Tucson, AZ 85724. (520) 626-7832; (800) 328-5868.

CALIFORNIA, HAWAII, AND NEVADA

All courses and meetings listed are approved for Category I credit toward the CMA Certificate in CME. To list accredited courses here, please send information at least two months in advance to Paulette Richardson, Continuing Medical Education, California Medical Association, PO Box 7690, San Francisco 94120-7690; or phone (415) 882-3387. For more information on accreditation or certification, please write to the above address.

ALLERGY/IMMUNIZATION

August 13–15, 1999—**A Midsummer Night's Wheeze.** California Society of Allergy, Asthma and Immunology at La Costa Resort and Spa, Carlsbad, CA. 12 hrs. $145-$199. Contact: CSAAI Conference Management at (714) 828-8022.

ANESTHESIOLOGY

November 5–7, 1999—**11th Annual Anesthesiology Update.** Monterey Plaza, Monterey, California. Contact (916) 734-5390.

CARDIOLOGY

July 25-29, 1999—**Nineteenth Annual Current Concepts in Primary Care Cardiology.** UC Davis School of Medicine, Division of Cardiovascular Medicine. Granlibakken Conference Center, Tahoe City, CA . Contact: Kimber Chavez, Program Representative at (916) 734-1394 or kimber.chavez@ucdmc.ucdavis.edu.

October 13-17, 1999—**Coronary Interventions 1999.** Scripps Clinic at Hilton La Jolla Torrey Pines, San Diego. Contact: Jill Hofmans, Conference Services Supervisor, Scripps Clinic. Dept. of Academic Affairs, 403C. 10666 N. Torrey Pines Rd., La Jolla, CA 92037; (619) 554-8556; fax (619) 554-6310.

DERMATOLOGY

May 23–26, 1999—**Practical Dermatology for the Primary Care Physician, Las Vegas, NV.** Sponsored by Continuing Medical Education Associates. To be held at the Caesars Palace, Las Vegas, NV. Method: AV, L, SB, W. 20 hrs credit: AMA, AOA, AAFP. $575. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

EMERGENCY MEDICINE

May 6–7, 1999—**Challenges in Pediatric Emergency Medicine.** Harrah's, Las Vegas, NV. Contact: CEME, 5330 Primrose Drive, Suite 250, Fair Oaks, CA 95628. (800) 651-2363.

May 13–16, 1999—**Outdoor Emergency Medicine, Scottsdale, AZ.** Sponsored by Continuing Medical Education Associates. Marriott Camelback Inn, Scottsdale, AZ. Method: AV, L, SB, W. 32 hrs credit: AMA, AOA, AAFP. $750. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

May 20–21, 1999—**High Risk Emergency Medicine.** Harrah's, Las Vegas, NV. Contact: CEME, 5330 Primrose Drive, Suite 250, Fair Oaks, CA 95628. (800) 651-2363.

June 3–4, 1999—**Improving Emergency Department Patient Satisfaction and Reducing Length of Stay.** Holiday Inn Chicago City Centre, Chicago, IL. Contact: CEME, 5330 Primrose Drive, Suite 250, Fair Oaks, CA 95628. (800) 651-2363.

August 16–19, 1999—**National Emergency Medicine Board Review.** American College of Emergency Physicians at Harrah's Las Vegas, NV. Mon–Thurs. 40 hrs. $895. Contact: Center for Emergency Medical Education (800) 651-CEME (2363).

October 3-5, 1999—**Northern California Trauma Center Conference.** UC Davis at Hyatt Regency, Sacramento. Contact: UC Davis fax (916) 734-4298.

ENDOCRINOLOGY

October 22–24, 1999—**Clinical Endocrinology for Primary Care Physicians.** Tropicana, Las Vegas, NV. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; (800) 421-3756, Fax (303)798-5731.

ETHICS

September 22-25, 1999—**Legal Issues in Damaged Brain Injury Cases.** UC Davis at Westin St. Francis Hotel, San Francisco, CA. Contact: UCD (916) 734-5390.

FAMILY PRACTICE/PRIMARY CARE

May 14-16, 1999—**Neurology for the Non-Neurologist.** Medical Education Resources at Bally's Las Vegas, NV. 11 hrs. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Ct., Ste. 500, Littleton, CO 80120-4569; (800) 421-3756.

May 14–18, 1999—**Primary Care Essentials, San Francisco, CA.** Sponsored by Continuing Medical Education Associates. Grand Hyatt on Union Square, San Francisco, CA. Method: AV, L, SB, W. 32 hrs credit: AMA, AOA, AAFP. $750. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

May 23–26, 1999—**Office Orthopedics and Bone Radiology for the Primary Care Physician.** CMEA at Caesar's Palace, Las Vegas, NV. Sun–Wed, 20 hrs, $575. Contact: Victoria Gonzalez, P.O. Box 270469, San Diego, CA 92198; (800) 993-2632 or (619) 674-5200.

May 23–26, 1999—**Practical Dermatology for the Primary Care Physician.** CMEA at Caesar's Palace, Las Vegas, NV 20 hrs. $575. Contact: Victoria Gonzalez, P.O. Box 270469, San Diego, CA 92198; (800) 993-2632 or (619) 674-5200.

June 5–7, 1999—**8th Annual Primary Care Treatment of Pain.** UC Davis at Tenaya Lodge at Yosemite Fish Camp, CA. Contact: UCD (916) 734-5390

June 13–18, 1999—**23rd Annual Fingers to the Toes Primary Care Orthopaedics.** UC Davis at Stanford Sierra Camp, near South Lake Tahoe. Contact: UCD (916) 734-5390

June 25-27, 1999—**Dermatology for the Non-Dermatologist.** Medical Education Resources at the Hyatt Regency Alicante, Anaheim, CA. 11 hrs.

Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Ct., Ste. 500, Littleton, CO 80120-4569; (800) 421-3756.

July 5–8, 1999—**Family Practice Board Review Course.** UCSF at Fairmont Hotel, San Francisco, CA. 25 hrs. $525–$575. Contact: Program Coordinator, Dept. Family and Community Medicine, 500 Parnassus Ave, MU-3E, SF, CA 94143-0900 or phone (415) 476-5250.

July 17-18, 1999—**3rd Annual Primary Care Pediatric Orthopedics.** Valley Children's Hospital at Doubletree Hotel, Monterey. 8 hours. $150. Contact: William Hennrikus (559) 353-5944.

July 23-24, 1999—**Controversies in Women's Health.** UCLA at Disneyland Hotel. 12 hours. $75-125. Contact: Jean Abbott (310) 312-0531.

July 25–29, 1999—**19th Annual Current Concepts in Primary Care Cardiology.** UC Davis at Granlibakken Conference Center, Tahoe City, CA. Contact: UCD (916) 734-5390.

July 30 – Aug 1, 1999—**Coronary Heart Disease Update.** Medical Education Resources at Tenaya Lodge, Yosemite, CA. 11 hrs. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Ct., Ste. 500, Littleton, CO 80120-4569; (800) 421-3756.

August 6-8, 1999—**Managing Respiratory Diseases.** Medical Education Resources at the Hyatt Regency Monterey, CA. 11 hrs. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Ct., Ste. 500, Littleton, CO 80120-4569; (800) 421-3756.

August 20-22, 1999—**Primary Care Medicine.** Scripps Clinic at Coronaro Island Marriott Resort, San Diego. 16 hours. Contact: Cheryl Trinidad, conference Coordinator, Scripps Clinic, Dept. of Academic Affairs, 403C, 10666 N. Torrey Pines Rd., La Jolla, CA 92037; phone (619) 554-8556; fax (619) 554-6310.

October 2-4, 1999—**7th Annual Western Retreat: Practical Primary Care.** Scripps Clinic at Monterey Marriott. 12 hours. Contact: Cheryl Trinidad, conference Coordinator, Scripps Clinic, Dept. of Academic Affairs, 403C, 10666 N. Torrey Pines Rd., La Jolla, CA 92037; phone (619) 554-8556; fax (619) 554-6310.

October 22-24, 1999—**Clinical Endocrinology for Primary Care Physicians.** Medical Education Resources at the Tropicana Hotel in Las Vegas, NV. 11 hours. Contact: MER Linda Main, Meeting Coordinator, 1500 West Canal Ct., Ste. 500, Littleton, CO 80120-4569; (800) 421-3756.

October 28-31, 1999—**11th Annual CME/Golf Meeting.** Nevada Academy of Family Physicians at The Orleans Hotel & Casino, Las Vegas, NV. Contact: Barbara Bolling, NAFP, P.O. Box 27713, Las Vegas, NV 89126-1713. (702) 228-5852; nafplvbb@aol.com

GERIATRICS

April 30, 1999—**Geriatrics in the New Millennium: Innovative Solutions to Old Problems.** UC Davis at UC Davis Cancer Center Auditorium. 7 hours. $100. Contact: Office of CME, UC Davis Medical Center, 2315 Stockton Blvd., Camellia Cottage, Room 1019, Sacramento, CA 95817. Phone: (916) 734-5390; Fax (916) 734-8966.

INTERNAL MEDICINE

August 22–27, 1999—**New Advances in Internal Medicine.** UC Davis at Embassy Suites, Monterey, CA. Contact UCD (916) 734-5390.

NEUROLOGY

May 14–16, 1999—**Neurology for the Non-Neurologist.** Bally's, Las Vegas, NV. CME 11 hrs Category 1. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; (800);421-3756; Fax (303)798-5731.

OB/GYN

April 28, 1999—**Mangement of Benign Uterine Conditions.** UC Davis at Cancer Center Auditorium, Sacramento, CA. 4 hrs. $50. Contact: UCD (916) 734-5390.

September 25–26, 1999—**Ultrasound Update: 1999.** Hilton Hotel, Sacramento, CA. (916) 734-5390.

December 10–12, 1999—**Issues in Women's Health.** Tropicana, Las Vegas, NV. CME 11 hrs Category 1. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; (800) 421-3756; Fax (303)798-5731.

OCCUPATIONAL & ENVIRONMENTAL

May 14–15, 1999—**Occupational and Environmental Medicine: 1999.** UC Davis at Cancer Center Auditorium, Sacramento, CA. Contact: UCD at (916) 734-5390.

August 5-6, 1999—**Occupational & Environmental Toxicology for the Health & Safety Professional.** UC Berkeley. Holiday Inn Bay Bridge, Emeryville, CA. Contact: Center for Occupational & Environmental Health, UC Berkeley, Richmond Field Station, 1301 S. 46th St., Bldg. 102, Richmond CA 94804; (510) 231-5645; http://socrates.berkeley.edu/~coehce/.

September 23-26, 1999—**Western Occupational Health Conference (WOHC).** American College of Occupational and Environmental Medicine and the Western Occupational and Environmental Medical Association at Monte Carlo Resort and Casino, Las Vegas, NV. 21 hours. Contact: Justine Abel, WOHC, 74 New Montgomery, Suite 230, San Francisco, CA 94105-3411. Phone: (415) 764-4083; Fax (415) 764-4915; woema@hp-assoc.com; www.woema.com.

ONCOLOGY

September 17-18, 1999—**5th Annual Cancer Research Symposium.** UC Davis at Cancer Center Auditorium, Sacramento, CA. Contact: Office of CME, UC Davis Medical Center, 2315 Stockton Blvd., Camellia Cottage, Room 1019, Sacramento, CA 95817. Phone: (916) 734-5390; Fax (916) 734-8966.

October 14-16, 1999—**23rd Annual Physicians Cancer Symposium.** Scripps Health, Stevens Cancer Center, San Diego, CA at La Jolla Hyatt Regency Hotel. 16.5 CME hours. Contact: Ruthanne Crawford, Stevens Cancer Center, Scripps Memorial Hospital 9888 Genesee Avenue, La Jolla, CA 92037. Phone: (619) 626-6756; Fax (619) 626-6793; racrawford@ch2.edu.

October 14-16, 1999—**19th Annual Nurses Cancer Symposium**. Scripps Health, Stevens Cancer Center, San Diego, CA at La Jolla Hyatt Regency Hotel. 18 contact hours. Contact: Ruthanne Crawford, Stevens Cancer Center, Scripps Memorial Hospital 9888 Genesee Avenue, La Jolla, CA 92037. Phone: (619) 626-6756; Fax (619) 626-6793; racrawford@ch2.edu.

OPHTHALMOLOGY

May 21, 1999—UC **Davis Annual Ophthalmology Symposium.** UC Davis at the Hilton Hotel, Sacramento, CA. Contact: UCD (916) 734-5390.

June 12, 1999—**Pearls of Ocular Therapy.** Scripps Clinic at Scripps Clinic, La Jolla, CA 6.5 hours. Contact: Jill Hofmanns, Conference Services Supervisor, Dept. of Academic Affairs, 403C, 10666 No. Torrey Pines Rd., La Jolla, CA 92037. Phone: (619) 554-8556; Fax (619) 554-6310.

ORTHOPEDICS

June 13–18, 1999—**23rd Annual Fingers to the Toes Primary Care Orthopaedics.** Stanford Sierra Camp, near South Lake Tahoe, Fallen Leaf Lake, CA. Contact (916) 734-5390.

PEDIATRICS

May 6–8, 1999—**Advances and Controversies in Clinical Pediatrics.** UCSF at Ritz-Carlton Hotel on Nob Hill, San Francisco, CA. Contact: UCSF (415) 476-5808 or Fax (415) 502-1795.

May 17–19, 1999—18th Annual Conference on Child Abuse and Neglect. **UC Davis at the Radisson Hotel, Sacramento, CA. 21 hrs. $195. Contact: UCD at (916) 734-5390.**

KEY TO ABBREVIATIONS

DREW:	Charles R. Drew Postgraduate Medical School, Office of Continuing Medical Education, (213) 563-4800.
LLU:	Loma Linda University, Continuing Medical Education Programs, (909) 824-4963.
STAN:	Stanford University, Postgraduate Education, (415) 723-5594.
UCD:	University of California, Davis, Office of Continuing Medical Education, (916) 734-5390.
UCI:	University of California, Irvine, Memorial/UCI Center for Health Education, (714) 824-5926.
UCLA:	University of California, Los Angeles, Continuing Education in Medicine and Health Sciences, (310) 794-2620.
UCSD:	University of California, San Diego, Office of Continuing Medical Education, (619) 534-3940.
UCSF:	University of California, San Francisco, Extended Programs in Medical Education, (415) 476-4251.
USC:	University of Southern California, Postgraduate Division, (800) USC-1119.

June 4-7, 1999—**Pediatric Environmental Health: Putting It Into Practice**. Children's Environmental Health Network. Westin St. Francis, San Francisco, CA. $250-350. Contact Children's Environmental Health Network, (510) 597-1393 x 14 or cehn@cehn.org.

July 16–17,1999—**Seventh Annual Pediatric Update.** Sponsored by Lucile Packard Children's Health Services at Stanford and faculty from UCSF and Stanford Schools of Medicine. Lucile Packard Children's Hospital. Contact: Elinor Meyer, Continuing Medical Education and Physician Relations Department, Lucile Packard Children's Hospital, 725 Welch Road, Palo Alto,CA 94304 (650) 497-8554.

PHYSICAL MEDICINE AND REHABILITATION

June 5-6, 1999—**Annual Meeting of California Physical Medicine and Rehabilitation**. CPMR at Radisson Hotel, Santa Barbara, CA. 13 hours. Contact: CSIM, (659) 573-6082.

PRIMARY CARE

June 5–7, 1999—**8th Annual Primary Care Treatment of Pain.** Tenaya Lodge at Yosemite, Fish Camp, CA. (916) 734-5390.

July 25–29, 1999—**19th Annual Current Concepts in Primary Care Cardiology.** Granlibakken Conference Center, Tahoe City, CA. (916) 734-5390.

October 22–24, 1999. **Clinical Endocrinology for Primary Care Physicians.** Tropicana, Las Vegas, NV. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; (800) 421-3756; Fax (303) 798-5731.

RADIOLOGY

September 25-26, 1999—**Ultrasound Update: 1999**. UC Davis at Hilton Hotel, Sacramento, CA. Contact: UCD (916) 734-5390.

RESPIRATORY

Managing Respiratory Disease—April 23–25, 1999–Las Vegas, NV; June 11–13, 1999–San Francisco, CA; August 6–8, 1999–Monterey, CA. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569 (800)421-3756 Fax (303)798-5731.

SURGERY

April 24, 1999—**3rd Annual Organ Transplant Conference.** UCD at Cancer Center Auditorium, Sacramento, CA. Contact UCD (916) 734-5390.

May 27–29, 1999—**2nd Annual Current Issues in Anatomic Pathology –1999.** UCSF at Mark Hopkins Intercontinental Hotel, SF. 19.5 hrs. $595. Contact: UCSF (415) 476-5808.

June 23-26, 1999—**16th Annual San Diego Shoulder Arthorscopy/Autoclasty Course.** Tri City Medical Center at Hyatt Regency La Jolla. 28.25 hours. $1650. Contact: Rebecca Quiring, Course Coordinator, 3905 Waring Road, Oceanside, CA 92056.Phone (760) 940-2066.

GENERAL/MULTIDISCIPLINARY

April 23–25, 1999—**Physician Leadership Program.** California Academy of Family Physicians at Claremont Hotel, Berkeley, CA. 20 hrs. $1245–$1395. Contact: Laura Johnson Morasch (415) 394-9121. Web: www.familydocs.org/Orgs?hcli.html E-mail: HCLI@familydocs.org.

April 28–May 8, 1999—**Blue Water Medical Seminar.** Tri City Medical Center at Baja California aboard Royal Star Sportfisher. 20 hrs. $3300. Contact: Ronald Mcdak (760) 727-7863.

May 16–19, 1999—**Alternative Medicine, Scottsdale, AZ.** Sponsored by Continuing Medical Education Associates. Marriott Camelback Inn, Scottsdale, AZ. Method: AV, L, SB, W. 20 hrs credit: AMA, AOA, AAFP. $575. Contact: Victoria Gonzales, P.O. Box 27049, San Diego, CA 92198. (800) 993-2632 or (619) 674-5200.

May 25 & 26, 1999—**BLS Instructor Course.** American Heart Association at San Leandro, CA. 11 hrs. $120. Contact: CPR Seminar (925) 754-7900.

June 22–29, 1999—**Wellness in Practice: Mindfulness-Based Stress Reduction in Mind/Body Medicine.** Enloe Medical Center at Mana L'ea Retreat Center, Maui. Contact: Maui Stress Reduction Retreats, Steve (530) 898-1495.

August 24–25, 1999—**BLS Instructor Course.** American Heart Association at San Leandro. 11 hrs. Contact: CPR Seminars (925) 754-7900.

October 15–17, 1999—**Physician Leadership Program.** California Academy of Family Physicians at Laurel Heights Conference Center, SF. 20 hrs. $1245–$1395. Contact: Laura Johnson Morasch (415) 394-9121. Web: www.familydocs.org/ Orgs?hcli.html (e-mail: HCLI@familydocs.org).

GENERAL

Converse in Spanish. October 1-4, 1999—Maricopa Health System at Scripps Memorial, San Diego. 36 hrs. $695. Contact: Rios Associates (619) 218-4875.

Masters of Medicine 1999. October 21-25, 1999—Continuing Medical Education Associates at Maui Marriott, Maui HI. 30 hours. $795. Contact: CMEA, P.O. Box 57072, Irvine, CA 92619-7072. Phone (800) 447-4474 or (949) 250-1008. Fax (949) 250-0445.

LOSS PREVENTION

September 22–25, 1999—**Legal Issues in Damaged Brain Injury Cases.** Westin St. Francis Hotel, San Francisco, CA. Contact (916) 734-5390.

HOME STUDY/SELF ASSESSMENT

California Physicians' Legal Handbook Series. California Medical Association. Contact: CMA, P.O. Box 7690, San Francisco 94120-7690. (800) 882-1262.

Breast Cancer, Early Detection and Control. Texas Medical Association. **CD ROM**. $70. 2 hrs. Contact: Texas Medical Association, (800) 880-1300; http://www.texmed.org/health_science/hs_poep.html

COLORADO

To list CME programs here, please send information at least two months in advance to: Mr Robert L. Kennedy, Denver Medical Society, 1850 Williams Street, Denver, CO 80218; or telephone (303) 377-1850. Brochures, course information, and registration forms are available from the contact person or organization.

Tuesday Noon Conferences—**Various Topics in Medicine.** Lutheran Medical Center, Wheat Ridge. Contact: Jean A. Kline, (303) 425-2951.

First Wednesday of Each Month—**Various Topics in Neurology.** Colorado Society of Clinical Neurologists. Contact: Colorado Society of Neurologists, (303) 449-3566.

Second Wednesday of Each Month—**Cardiovascular Education Series.** St Anthony Hospital at St Anthony Hospital, Denver. Contact: Rose Powell, (303) 629-3678.

April 30–May 2, 1999—**Dermatology For The Non-Dermatologist.** South Sea Plantation, Captiva Island, FL. Fee $375. Contact Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

April 30–May 2, 1999—**Clinical Endocrinology For Primary Care Physicans.** Hyatt Regency, New Orleans, LA. Fee $375. Contact Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

May 14–16, 1999—**Managing Respiratory Diseases.** Hilton Resort, Hilton Head, SC. Fee $375. Contact Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

June 17-19, 1999—**Issues in Women's Health**. Hyatt Regency, Grand Cayman. Contact Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

June 18-20, 1999—**Neurology For The Non-Neurologist.** Buena Vista Palace, Orlando, FL. Fee $375. Contact Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

June 24-26, 1999—**Clinical Endocrinology For Primary Care Physicans.** Sonesta Beach Resort, Bermuda. Fee $375. Contact Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

June 25-27, 1999—**Coronary Heart Disease Update.** Sheraton Fiesta Beach Resort, S. Padre Island, TX. Fee $375. Contact Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569. (800) 421-3756, (303) 798-9682 or Fax (303) 798-5731.

CONTACT INFORMATION

U of Colo—Contact: University of Colorado Health Sciences Center, School of Medicine, Office of Continuing Medical Education, 4200 E 9th Ave, Denver 80262. (303) 372-9050 or (800) 882-9153; Fax (303) 372-9065.

IDAHO

To list CME programs here, please send information at least two months in advance to: Ada County Medical Society, Inc. 305 W. Jefferson, PO Box 2668, Boise, Idaho 83701. (208) 336-2930. Brochures, course information, and registration forms are available from the contact person or organization.

June 10-12, 1999—**22nd Annual Snake River Medical Forum**. St. Joseph Regional Medical Center at Red Lion Hotel, Lewiston, ID. Contact: Koleen Wagner at (208) 799-5460.

NEW MEXICO

Information, requests for accreditation, and items to be listed should be sent to the chair of the CME Committee, New Mexico Medical Society, 7770 Jefferson, Suite 400, Albuquerque, NM87109, at least two months in advance. For information on CME accreditation or on the CME requirements of the New Mexico Board of Medical Examiners, please write to the above address or call (505) 828-0237.

NOTE: Course information in the following listing is subject to change on occasion. Check with the sponsoring institution for current details.

Every First and Third Tuesday—**Building and Implementing Clinical Practice Guidelines at the Point of Care.** Contact: Thomas A. Naegele, DO, (505) 275-7267.

April 28–30, 1999—**The Fourth Annual Clinical Cardiology Management and Diagnostic Dilemmas.** Eldorado Hotel, Santa Fe, NM. 17 Category 1 AMA. Contact: Registration Secretary, American College of Cardiology, 9111 Old Georgetown Rd, Bethesda, MD 20814-1699 (800) 253-4636, ext. 695.

July 30–August 1, 1999—**Neurology for the Non-Neurologist.** Eldorado Hotel, Sante Fe, NM. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; (800) 421-3756; Fax (303)798-5731.

SATELLITE COURSES

Contact: Joe Treat or Jim Cato, Immunization Program, (505) 827-2366.

CONTACT INFORMATION

UNMSOM—University of New Mexico School of Medicine, Office of CME, PO Box 713, Albuquerque 87131. (505) 277-3942.

UTAH

All courses listed meet the criteria for Category 1 of the Physician's Recognition Award of the AMA. To list AMA Category 1 CME courses, send information at least two months in advance to the Office of Continuing Medical Education, 540 East Fifth South, Salt Lake City, UT 84102; or phone (801) 355-7477. For information on CME accreditation, please write the CME office at the above address. NOTE: Course information in the following listing is subject to change on occasion. Check with the sponsoring institution.

MEDICAL GRAND ROUNDS

Weekly—**Grand Rounds in Internal Medicine, Psychiatry, OB/GYN, and Pediatrics.** Contact: UUSM.

Weekly—**Pediatric Grand Rounds.** Contact: PCMC.

WASHINGTON

The listing of continuing medical education programs in Washington state is compiled by the Washington State Medical Association. To list Category 1 programs here, please send information at least two months in advance to Continuing Medical Education, Washington State Medical Association, 2033 Sixth Avenue, Suite 1100, Seattle, WA98121; or phone (206) 441-9762 or (800) 552-0612.

Brochures and registration forms are available from the contact person or organization listed at the end of each course or in the list of course sponsors and contact information.

COURSE SPONSORS AND CONTACT INFORMATION

CME HARBORVIEW—Contact: Gayle Splater, Cytology Continuing Education, Dept. of Pathology, Harborview Medical Center, 325 Ninth Ave, Seattle, WA98104. (206) 223-5953.

PCMS CME—Contact:Executive Director, College of Medical Education, 705 S Ninth, No. 203, Tacoma, WA 98405. (206) 627-7137.

U/W (UNIVERSITY OF WASHINGTON)—Contact: U/W School of Medicine, Div. of CME, SC-50, Seattle, WA98195. (206) 543-1050.

VMMC (VIRGINIA MASON MEDICAL CENTER)—Contact: Linda Orgel, Division of Continuing Medical Education, Virginia Mason Medical Center, POBox 900, Seattle, WA 98111. (206) 340-2058.

WSMA—Washington State Medical Association, Continuing Medical Education, 2033 Sixth Ave, Ste 1100, Seattle, WA 98121. (206) 441-9762.

WYOMING

All courses meet the criteria for Category 1 of the Physician's Recognition Award of the AMA. To list AMA Category 1 CME courses here, send information at least two months in advance to the Medical Education Committee, Wyoming Medical Society, P.O. B ox 4009, Cheyenne, WY 82009; email skeefe@wyomed.org; phone 307 634-2424; Fax 307 632-1973.

June 16-18, 1999—**Annual Meeting/Scientific Session: Wyoming Medical Society**. Jackson Lake Lodge, Moran WY. Contact: Susie Wacker, P.O. Box 4009, Cheyenne, WY 82003 or swacker@wyomed.org.

August 30-September 1, 1999—**Tutorial in the Tetons**. American College of Cardiology at Jackson Lake Lodge, Moran WY. 14.5 CME. Contact: Registration Secretary, Extramural Programs Dept., American College of Cardiology, 9111 Old Georgetown Rd., Bethesda, MD 20814-1699; (800) 253-4636. ext. 695. Fax: (301) 897-9745.

OTHER CME OPPORTUNITIES

Brochures and registration forms are available from the contact person or organization listed at the end of each course or in the list of course sponsors and contact information.

April 28-May 2, 199 — **32nd Annual Spring Conference.** Sheraton Seattle Hotel & Towers, Seattle, Washington. Contact: Ray Rosetta, Meetings and Programs Director, Society of Teachers of Family Medicine, 8880 Ward Parkway, Kansas City, MO 64114. Phone (800) 274-2237, ext. 4512.

May 14, 1999—**Setting a New Standard of Care: An Office-Based Management Program for Hyperlipidemia in a Managed Care Environment.** National Association of Managed Care Physicians. Hyatt Crystal City, Arlington, VA. Contact: National Association of Managed Care Physicians. (804) 527-1905.

June 11-13, 1999—**41st Annual Scientific Meeting of the American Association for the Study of Headache.** Marriott Copley Place, Boston, MA. Contact: Melissa Bishop, (609) 423-3195; Fax (609) 423-0082.

July 18-21, 1999—**Eighth National Alzheimer's Disease Education Conference**. Alzheimer's Disease and Related Disorders Association at Long Beach Convention Center, Long Beach, CA. Contact: Nicolle Heller, Alzheimer's Association, (312) 335-4037; Nicolle.Heller@alz.org.

September 30- October 2, 1999—**7th Annual Conference on Management of the Tinnitus Patient**. University of Iowa College of Medicine at Medical Alumni Auditorium, Room E331 UIHC, The University of Iowa Hospitals and Clinics, Iowa City, IA. Contact: Cheryl Schlote, Phone: (319) 384-9757; Fax (319) 353-6739; cheryl-schlote@uiowa.edu.

NOTICE

State Associations should send their CME listings for publication to:

Catherine Nancarrow, Editorial Manager
The Western Journal of Medicine
P.O. Box 7690
San Francisco, CA 94120-7690

(415) 974-5977 • Fax (415) 882-3379

Letter From the Editors

Next Month

WJM

The same high standards — A whole new approach.

In next month's issue, *The Western Journal of Medicine* will acquire a new name: *WJM*. It will also have a new look. The new *WJM* is dedicated to being a voice for health care providers in Western states, and a forum for the issues that are important to them. It will be informative, evidence-based, enjoyable, and readable. *WJM* will emphasize primary care, appreciate specialty care, and be open to new ideas about the practice of medicine.

The new journal will maintain the high standards set by the old *Western Journal of Medicine* for the publication of high quality peer-reviewed research. Some of the editorial staff of the old *Western Journal* will continue to work with us, but we will also be asking new contributors to help us explore and debate controversial and significant issues in health care.

We strive to offer practical, reliable information for clinicians, and new sections have been established for that purpose. "Medicine Cabinet" will offer pharmacy tips from pharmacists. "Evidence-Based Case Reviews" will provide extensively referenced guides to the management of common and uncommon clinical problems. "Research Digest" will offer summaries of important recent research.

We also hope to be the place our readers turn for news of what is happening in health care in Western states and provinces. To that end, our "News and Features" section will offer in-depth reporting by journalists, as well as brief synopses of medical events that have been receiving attention.

In our "Media Watch" section, we will criticize and comment on how the media covers health care. We will provide a space for physicians and patients to describe and reflect on their own personal experiences in the health care system in a section called "Speaker's Corner." Remarkable programs in health care and medical education will be described in the section "West of the Rockies," and new columnists will offer us a regular perspective from the Southwest and the Northwest.

The new *WJM* espouses the belief that the medicine of the millenium cannot be described in words alone. Medical and nonmedical images will be found throughout the journal. Radiographic imagery will be presented in a new section called "Med.Pix," while the cover and the last page of the journal will always be reserved for evocative images by Western photographers.

A journal is first and foremost about communication. The new *WJM* aims for improved communication with our readers and our contributors. We are asking readers to be in touch with us not only via the mail, but also via the rapid response mechanism that will be available on the journal's website some time in the next few months.

We are also asking readers to submit clinical questions for the section, "Curbside Consult," and we will find experts to respond. As for our contributors, we are working hard to lessen the time from submission to publication while still ensuring thorough review by outside experts and inside editorial staff. We realize that this is crucial to attracting high-quality submissions and to providing information to our readers in a timely fashion.

Keep an eye out for your May copy of the journal and let us know your thoughts once you've seen it.

MICHAEL S. WILKES, MD, PHD
Editor

MIRIAM SHUCHMAN, MD
Editor

Original Research

Methamphetamine Abuse and Emergency Department Utilization

JOHN R. RICHARDS, MD; STEPHEN W. BRETZ, MD; EMILY B. JOHNSON; SAMUEL D. TURNIPSEED, MD; B. TOMAS BROFELDT, MD; ROBERT W. DERLET, MD; *Sacramento, California*

Methamphetamine (MAP) abuse continues to increase worldwide, based on morbidity, mortality, drug treatment, and epidemiologic studies and surveys. MAP abuse has become a significant health care, environmental, and law enforcement problem. Acute intoxication often results in agitation, violence, and death. Chronic use may lead to infection, heart failure, malnutrition, and permanent psychiatric illness. MAP users frequently use the emergency department (ED) for their medical care. Over a 6-month period we studied the demographics, type, and frequency of medical and traumatic problems in 461 MAP patients presenting to our ED, which serves an area noted for high levels of MAP production and consumption. Comparison was made to the general ED population to assess use patterns. MAP patients were most commonly Caucasian males who lacked health insurance. Compared to other ED patients during this time, MAP patients used ambulance transport more and were more likely to be admitted to the hospital. There was a significant association between trauma and MAP use in this patient population. Our data suggest MAP users utilize prehospital and hospital resources at levels higher than the average ED population. Based on current trends, we can expect more ED visits by MAP users in the future.

(Richards JR, Bretz SW, Johnson EB, Turnipseed SD, Brofeldt BT, Derlet RW. Methamphetamine abuse and emergency department utilization. West J Med 1999; 170:198–202)

Methamphetamine (MAP) is a central nervous system (CNS) stimulant that has an extensive history of abuse since its advent 80 years ago. Illicit MAP use has been increasing steadily in the United States and is rapidly spreading worldwide. MAP is now the most common drug of abuse presenting to emergency departments (ED) in the western United States.[1] Intoxicated MAP patients often present with agitation, violence, and loss of self-control and represent a threat to themselves and caregivers.[2] Chronic MAP users often develop paranoia and lasting psychosis as well as deterioration of judgment and fine motor skills, which may predispose them to injury from moving vehicle accidents.[3,4] Chronic use also results in serious health problems including malnutrition, poor dentition, exhaustion, and systemic or soft-tissue infection from injecting MAP.[5] Criminal and violent behavior associated with MAP may lead to blunt and penetrating traumatic injury.[6,7] Patterns of use vary considerably and include occasional or sporadic use, to "bingeing" over a period of several days. Inevitably, increasing MAP abuse translates into more frequent ED visits by this population. To better appreciate the protean nature of MAP abuse, we reviewed ED visits by patients with positive toxicology screens for MAP to determine demographics, the relative frequency of associated medical and traumatic problems, and disposition. We also compared these variables with the remaining ED population to assess ED use patterns.

Materials and Methods

This study was done over a 6-month period from September 1996 through February 1997 at the University of California, Davis Medical Center, a large urban university hospital with an annual ED census of 70,000 visits. This hospital is a level I trauma center and represents the de facto public hospital for its urban geographic area, serving a population of 400,000 within the city limits and 1.5 million in the surrounding area. Our institution provides health care for a high proportion of uninsured patients and for those patients brought in by police from the street or from jail. Retrospective review of all patients presenting to the ED with a urine toxicology screen positive for MAP was performed. Charts were abstracted for

From the Division of Emergency Medicine, University of California, Davis Medical Center, Sacramento, California.

Presented at the First Asian Congress on Emergency Medicine, October 1998, Singapore.

Reprint requests to John R. Richards, MD, Division of Emergency Medicine, 2315 Stockton Boulevard, Sacramento, CA 95817 (e-mail: jrrichards@ucdavis.edu).

TABLE 1.— *Demographic Differences Between MAP and Non-MAP Patients**

	MAP n (%)	*non-MAP n (%)*	*OR (95% CI)*	*P*
Age ± SD (y)	34.9 ± 8.5	41.2 ± 13.6		< 0.001
Male	295 (64)	16,721 (52)	1.6 (1.4, 2.0)	< 0.001
Female	166 (36)	15,435 (48)	0.6 (0.5, 0.7)	< 0.001
Race				
Caucasian	341 (74)	16,399 (51)	2.7 (2.2, 3.4)	< 0.001
Hispanic	63 (13)	3,859 (12)	1.2 (0.9, 1.5)	0.3
African American	37 (8)	6,110 (19)	0.4 (0.3, 0.5)	< 0.001
Asian/Pacific Islander	18 (4)	5,576 (17)	0.2 (0.1, 0.3)	< 0.001
Native American	2 (1)	212 (1)	0.6 (0.2, 2.6)	0.7
Insurance				
None	375 (81)	17,685 (55)	3.6 (2.8, 4.5)	< 0.001
MediCal/MediCare	56 (12)	8,360 (26)	0.4 (0.3, 0.5)	< 0.001
HMO/MCO	20 (5)	4,823 (15)	0.3 (0.1, 0.4)	< 0.001
Self-pay	10 (2)	1,288 (4)	0.5 (0.3, 0.9)	0.06

*All findings significant at $P < 0.001$.
SD = standard deviation, HMO/MCO = health maintenance organization/managed care organization

patient demographics, insurance status, chief complaint, mode of arrival, vital signs, laboratory results, smoking habits, procedures, disposition, and outcome. The rapid urine toxicology screen for drugs of abuse, which detects cocaine, opiate derivatives, benzodiazepines, barbiturates, tetrahydrocannabinol, and phencyclidine, was processed on a CX-7 analyzer in the ED (Beckman Industries, Fullerton, California). Univariate statistical analysis was done using chi-square and unpaired Student *t* tests. Calculations were done with Stata 5.0. Data are reported as mean ± standard deviation (SD) unless otherwise stated. Statistical significance is assumed at a level $P \leq 0.05$. This study was approved by the human subjects review committee at our institution.

Results

A total of 461 patients were identified as having MAP on their urine toxicology screens. During the study period there were 3,102 total urine toxicology screens performed on ED patients and 32,156 total ED visits. Comparison of demographics between patients with positive toxicology screens for MAP and all others are presented in Table 1. The range of age for MAP patients was 3 to 67 years.

Concomitant drug use by MAP patients was also recorded. Tobacco use was documented in 413 MAP patients (90%). Ninety-two patients (20%) coingested ethanol, with an average blood level of 125 ± 32 mg/dl. Other drugs detected included opiates (n = 61, 13%), cocaine (n = 34, 7%), benzodiazepines (n = 21, 5%), tetrahydrocannabinol (n = 20, 4%), and phencyclidine (n = 2, 0.4%). With regard to mode of arrival, MAP patients were most likely to use ambulance transport (n = 319, 69%), followed by: brought in by self, family, or friend (n = 66, 14%); brought in by police (n = 56, 12%); and mental health facility transfer (n = 20, 4%). During this period there were 7,584 total ambulance transports to our institution. A significant difference in use of ambulance transport existed between MAP and non-MAP patients (69% versus 22%, $P < 0.001$).

Chief complaints and admissions are displayed in Table 2. A total of 268 MAP patients were admitted to the hospital from the ED (58%), followed by 89 who were discharged directly to home (19%). Sixty-three MAP patients were discharged to an inpatient psychiatric facility from the ED (14%), and 41 MAP patients went directly to jail (9%). During this period there were 7,074 admissions to the hospital from the ED. Difference in admission rates for MAP patients and non-MAP patients was significant (58% versus 22%, $P < 0.001$). Average stay for MAP patients was 2.8 ± 1.8 days, and 386 of the 461 MAP patients had two or more ED visits within the past 12 months.

A total of 172 MAP patients (37%) had injuries from trauma (Table 2), of which blunt trauma was most common. Mechanism of injury is demonstrated in Table 3. For the study period there were 6,753 trauma-related ED visits. A significant difference was noted between MAP patients and non-MAP patients for trauma-related complaints (37% versus 21%, $P < 0.001$). Fifty-three of 172 MAP patients (31%) with trauma required sedation for acute agitation.

The next most common presenting complaint for MAP patients was altered level of consciousness (Table 2). In this subgroup, 83 patients were acutely agitated. Sixteen were noted on the ED record to have hallucinations, of which 10 were of the visual and tactile sensation of insects crawling on the patient's body. None of these 10 patients were experiencing ethanol withdrawal at the time. Sixteen

TABLE 2.— *Chief Complaints and Hospital Admissions of MAP Patients*

Chief Complaint	*Total n (%)*	*Admissions n (%)*
n	*n* = 461	*n* = 268
Blunt trauma	152 (33)	112 (74)
Altered LOC	108 (23)	52 (48)
Abdomen pain	58 (13)	18 (31)
Suicide attempt	38 (8)	11 (29)
Chest pain	36 (8)	28 (78)
Skin infection	28 (6)	15 (54)
Penetrating trauma	20 (4)	18 (90)
Miscarriage	8 (2)	6 (75)
Ingestion	8 (2)	5 (63)
Headache	5 (1)	3 (60)

LOC = level of consciousness

patients had tonic-clonic seizures, of which 12 were new-onset. The remaining 9 were evaluated for syncope.

Thirty-eight patients were suicidal. The most common attempted mode of suicide was overdose (n = 22), followed by slash wounds to extremities (n = 10), and jumps from heights (n = 5). One patient attempted suicide by striking a brick to his head several times after injecting MAP. A total of 52 patients were brought in or placed on a 72-hour psychiatric hold while in the ED. There were 8 cases of oral ingestion of MAP, 7 of which were for evading police detection of MAP possession. The remaining patient was a 3-year-old boy who ingested some of his parents' MAP, which was lying on the floor.

Twenty-eight patients presented with skin infections from injecting MAP, including 21 with abscesses and 7 with cellulitis. All 21 abscesses required incision and drainage: 12 were performed in the ED under local anesthesia, and the remaining 9 were performed in the operating room. Of note, 18 of the 28 MAP patients with skin infections insisted that a "spider bit them."

Discussion

The demographics of MAP patients in this study correlate well with previous studies describing defined populations of MAP users. Baberg and colleagues screened inpatient psychiatric consultations at a university medical center and found that MAP use doubled over 6 years in a population with demographics similar to ours.[8] Bailey studied toxicology screens in university hospital patients and reported demographics similar to our data.[9] The typical user in our study was a Caucasian male in his early thirties with no health insurance. Thirty-six percent of MAP patients were female, however, and the use of MAP by females in general has been increasing.[1] Proposed reasons for this trend include the following short-term benefits of MAP use: increased wakefulness allowing for multiple jobs and overtime, weight loss, and enhanced sexual drive. Anderson and Flynn reported an estimated 7,000 MAP injectors in Sacramento County, of whom most are male, Caucasian, young, and employed.[10] A survey of adolescents by this same team found that MAP was the most commonly used drug after alcohol and marijuana, and 54% admitted using MAP at least once. A 10-year-old study by Derlet et al examined 127 cases of amphetamine toxicity in the ED, and this group found these patients presented with a wide range of complaints, of which altered mental status was foremost.[11] They found less associated trauma compared to our results.

A remarkable association between MAP use and injury from trauma existed in this study. Interpersonal trauma, including gunshot wounds, stabbings, and assaults, was responsible for a large number (n = 67) of ED visits (Table 3). The predisposition for violence and suicide from MAP abuse may account for the large proportion of these cases. This association has been investigated in previous studies.[6,7] Kratofil and colleagues described self-injury and mutilation by MAP users.[12] Logan reported a correlation between MAP and violent behavior in drivers arrested for driving under the influence of alcohol.[4] In another series by the same author, 146 deaths involving MAP were reviewed on autopsy, and 27% resulted from homicidal and 15% from suicidal violence.[7] A similar study from Spain also found a high percentage of violent deaths in MAP-positive autopsies.[13] Bailey and coworkers reported MAP presence in almost one-third of homicides and accidental overdoses in San Diego County.[14] In the subculture of MAP users, in which paranoia, poor judgment, predisposition for violence, and access to weapons coexist, any potential misunderstanding or disagreement, however insignificant, may lead to interpersonal violence.

The deleterious effect of MAP on psychomotor and cognitive skills has been well documented. The most notable consequence of this effect is an increased incidence of moving vehicle accidents and falls. In a series of moving vehicle accidents described by Logan et al, poor coordination and judgment was responsible for the majority of crashes, and typical driving behaviors included drifting out of the lane of travel, erratic driving, weaving, speeding, drifting off the road, and high speed collisions.[4] The majority of MAP patients with blunt trauma in our study were involved in car crashes and other moving vehicles, including 2 MAP users who were riding bicycles and crashed into each other (Table 3). Crouch and coworkers investigated fatal truck crashes over a one-year period and found that an alarmingly high percentage tested positive for MAP postmortem.[15] Although MAP does significantly extend periods of wakefulness, this benefit is quickly negated by poor task functioning. Wiegmann and colleagues studied the effect of MAP on cognitive processing, which deteriorated considerably with extended periods of wakefulness induced by MAP.[16]

Chronic MAP use also has been associated with the development of schizophreniform mental illness, which

TABLE 3.—*Mechanism of Trauma for Injured MAP Patients*

	n (%)
Blunt	*n* = 152
Auto/truck crash	64 (42)
Assault	47 (31)
Fall	16 (11)
Auto versus pedestrian	10 (7)
Auto versus bike	9 (6)
Motorcycle crash	5 (3)
Bike versus bike	1 (1)
Penetrating	*n* = 20
Gunshot	11 (55)
Stabbing	9 (45)

may be permanent.[17] The paranoia accompanying MAP use is well documented. In one study only 32% of patients admitted to using MAP when confronted with their positive toxicology results.[2] A large number of MAP injectors in our study (n = 18) claimed that their soft-tissue infections were the result of a "spider bite." For 10 patients in this study, note was made in each patient's record that the patient stated someone may have "slipped something in my drink" or "spiked my drink."

The association of MAP use and smoking was profound in our study. This association has been previously described.[10] The combination of nicotine and MAP results in a byproduct, cyanomethylmethamphetamine. In one study by Sekine et al,[18] this compound was demonstrated to have even greater psychostimulant effects than MAP alone.

Our study population also demonstrated a strong propensity for ethanol use. Slawecki and colleagues studied the effect of MAP on ethanol use and found MAP to increase the craving for ethanol and the volume consumed.[19] Concomitant ethanol ingestion further compromises the already impaired coordination and judgment of MAP users who operate moving vehicles.

Users who inject MAP intravenously expose themselves to a large number of serious health problems.[5] Human immunodeficiency virus (HIV), viral hepatitis, endocarditis, and pulmonary abscess may result from MAP injectors using poor needle hygiene.[10] Molitor and colleagues reported that MAP users, especially those who administer MAP by injection, indulge in higher-risk sexual behavior when compared to other users of illicit drugs and are more likely to have a sexually transmitted disease.[20]

The byproducts of clandestine MAP synthesis are extremely hazardous, and there is little or no quality control for the finished product. In Oregon, many injectors developed lead poisoning from a contaminated batch of MAP.[21]

This study had several limitations. The study is a retrospective review. No protocol existed for selection of patients for urine toxicology screening, which may have biased our results. Our institution is located in an area noted for high levels of MAP production and consumption and provides health care to a large number of uninsured patients. Studies drawn from toxicology results also may underestimate the frequency of drug abuse, because patients who admit to using illicit drugs often are not tested. The urine toxicology test was not followed by more specific gas chromatography confirmation. Although it is possible that some of the toxicology results in this study may have been from false positives or iatrogenic medication, we believe this number to be small and did not measurably affect our results. There were no indications in reviewing patient records that positive toxicology screens resulted from legitimate intake of over-the-counter medications or from prescribed amphetamine derivatives. Definitively linking MAP with the patient's chief complaint was not possible because the amount of time elapsed between last MAP dose and presentation to the ED could not be established.

Conclusion

Methamphetamine abuse patients presenting to the ED tend to be young Caucasian males, tobacco smokers, and have no health insurance. Compared to the average ED patient, MAP patients use ambulance transport at a much higher rate and are more likely to be admitted to the hospital. A significant association between MAP patients and trauma also existed. Methamphetamine abuse will continue to worsen if current trends prevail. Clinicians must be aware of the variable nature of MAP abuse and its deleterious effect on patients' mental and physical health.

REFERENCES

1. Centers for Disease Control and Prevention. Increasing morbidity and mortality associated with abuse of methamphetamine—United States, 1991–1994. MMWR Morb Mortal Wkly Rep 1995; 44:882–886

2. Richards JR, Derlet RW, Duncan DR. Methamphetamine toxicity: treatment with a benzodiazepine versus a butyrophenone. Eur J Emerg Med 1997; 4:130–136

3. Morgan JP. A lasting vulnerability to psychosis in patients with previous methamphetamine psychosis. Ann NY Acad Sci 1992; 654:160–170

4. Logan BK. Methamphetamine and driving impairment. J Forensic Sci 1996; 41:457–464

5. Hando J, Topp L Hall W. Amphetamine-related harms and treatment preferences of regular amphetamine users in Sydney, Australia. Drug Alcohol Depend 1997; 46:105–113

6. Ellinwood E. Assault and homicide associated with amphetamine abuse. Am J Psychiatry 1971; 127:90–95

7. Logan BK, Fligner CL, Haddix T. Cause and manner of death in fatalities involving methamphetamine. J Forensic Sci 1998; 43:28–34

8. Baberg HT, Nelesen RA, Dimsdale JE. Amphetamine use: return of an old scourge in a consultation psychiatry setting. Am J Psychiatry 1996; 153:789–793

9. Bailey DN. Amphetamine detection during toxicology screening of a university medical center patient population. Clin Tox 1987; 25:399–409

10. Anderson R, Flynn N. The methamphetamine–HIV connection in Northern California. In Klee H (Ed). Amphetamine Misuse: International Perspectives on Current Trends. Amsterdam, Harwood Publishers, 1997, pp 1–18

11. Derlet RW, Rice P, Horowitz BZ, Lord R. Amphetamine toxicity: experience with 127 cases. J Emerg Med 1987; 7:157–161

12. Kratofil PH, Baberg HT, Dimsdale JE. Self-mutilation and severe self-injurious behavior associated with amphetamine psychosis. Gen Hosp Psychiatry 1996; 18:117–120

13. Lora-Tamayo C, Tena T, Rodriguez A. Amphetamine derivative related deaths. Forensic Sci Int 1997; 85:149–57

14. Bailey DN, Shaw RF. Cocaine and methamphetamine-related deaths in San Diego County 1987: homicides and accidental overdoses. J Forensic Sci 1989; 34:407–422

15. Crouch DJ, Birky MM, Gust SW, et al. The prevalence of drugs and alcohol in fatally injured truck drivers. J Forensic Sci 1993; 38:1342–1353

16. Wiegmann S, McKay DL, Neri DF, et al. Methamphetamine effects on cognitive processing during extended wakefulness. Int J Aviation Psychol 1996; 6:379–397

17. Bell DS. The experimental reproduction of amphetamine psychosis. Arch Gen Psychiatry 1973; 29:35–40

18. Sekine H, Nagao S, Kuribara H, Nakahara Y. Behavioral effects of N-cyanomethylmethamphetamine, a product derived from smoking methamphetamine with tobacco, in mice and rats. Pharm Biochem Behav 1997; 57:167–172

19. Slawecki CJ, Samson HH, Chappell A. Intranucleus accumbens amphetamine infusions enhance responding maintained by a stimulus complex paired with oral ethanol. Pharm Biochem Behav 1997; 58:1065–1073

20. Molitor F, Truax SR, Ruiz JD, Sun RK. Association of methamphetamine use during sex with risky sexual behaviors and HIV infection among non-injection drug users. West J Med 1998; 168:93–97

21. From the Centers for Disease Control. Lead poisoning associated with intravenous-methamphetamine use—Oregon, 1988. MMWR Morb Mortal Wlky Rep. Taken from: JAMA 1990; 263:797–799

Original Research

Fracture Epidemiology and Control in a Developmental Center

GHAN-SHYAM LOHIYA, MD, MS, *Costa Mesa and Irvine, California*; FRANCIS M. CRINELLA, PHD, *Irvine, California*; LILIA TAN-FIGUEROA, MD; SHIRLEY CAIRES, PHN, CIC, *Costa Mesa, California*; SONIA LOHIYA, *Newport Beach, California*

During 3.5 years, 182 fractures occurred among 994 residents of a developmental center. The fracture rate was 5.2 per 100 person-years (1.7 times greater than the rate in the US population). Fracture rate was significantly greater in residents with: epilepsy, older age, male gender, white race, independent ambulation, osteoporosis, and residence in intermediate care (versus skilled nursing) units; it was not affected by severity of mental retardation. Hand and foot bones were fractured in 58% of cases. Femur fracture occurred in 13 cases (7%). Fracture was caused by a fall in 41 cases (23%); its cause was indeterminable in 105 cases (58%). Fractures, occurring without significant injury, may be an important cause of preventable disability in this population. Control measures are suggested.

(Lohiya G-S, Crinella FM, Tan-Figueroa L, Caires S, Lohiya S. Fracture epidemiology and control in a developmental center. West J Med 1999; 170:203–209)

In 1997, there were approximately 146,517 people with developmental disabilities (DD) in California; 4,102 of them resided in a developmental center.[1] To maintain the quality of life for individuals with DD, it is important to prevent acquisition of new disabilities. Attention should therefore be focused on fractures because they can cause substantial morbidity, and many can be readily prevented. Per US data, an average fracture requires active medical care in 97% of cases, and leads to 53 restricted-activity days, 16 bed days, 33 work-loss days, and 8 school-loss days.[2]

Fractures appear to be common in individuals with DD, especially in those with epilepsy.[3–9] To reduce fracture-related disability, it is crucial to identify factors that contribute to this predisposition. Only one study has been published describing the epidemiology of fractures in people with DD.[2] That study, however, was biased, as 98% of its subjects had epilepsy, and were therefore prone to fractures.[3–9] We present the epidemiology of fractures in a center whose residents are more representative of the general population of people with DD, the majority of whom have no epilepsy.

Method

This study was conducted at Fairview Developmental Center, one of five long-term care facilities in California for people with DD. Its features have been described previously.[10] Consistent with a national trend for community care of people with lesser DD,[11] and the Coffelt settlement requiring the same,[12] the Fairview Developmental Center resident census has decreased to 40% of its licensed capacity since its dedication in 1961. Consequently, current residents are older, with more severe medical or behavioral impairments.[11]

Licensed staff routinely monitor all residents for injury (pain, swelling, bruising, refusal to use a part). All suspected injuries are evaluated by a physician and radiographed, then a special incident report is prepared in compliance with state regulation. All fractures are listed on a fracture log. We reviewed records of all persons who had a fracture during the preceding 3.5 years.

For all residents, information was obtained about age, gender, race, level of mental retardation, care level (skilled nursing or intermediate care), mobility (ability to move about independently with or without a wheelchair), clinical diagnosis of osteoporosis or epilepsy, and cause of fracture. If a single injury fractured multiple bones, each fracture was counted separately. No resident received alendronate or electroconvulsive therapy. Common anticonvulsants prescribed for epileptics were phenobarbital, phenytoin, carbamazepine, valproic acid, and gabapentine.

From the Fairview Developmental Center, Costa Mesa, California (Drs Lohiya and Tan-Figueroa and Ms Caires); the Department of Pediatrics, University of California, Irvine, California (Drs Lohiya and Crinella); and the Eleventh Grade, Corona Del Mar High School, Newport Beach, California (Ms Lohiya).

This study was supported by Fairview Developmental Center, Costa Mesa, CA, and the Department of Developmental Services, State of California. Opinions expressed herein are those of the authors and do not represent the position of either agency.

Reprint requests to: G. Lohiya MD, MS; Public Health Officer, Fairview Developmental Center, 2501 Harbor Boulevard, Costa Mesa, CA 92626.

Figure 1.—Radiograph illustrating osteoporosis. The bold paired arrows point to a compression fracture of a vertebral body. There is loss of trabecular bone causing accentuation of the vertebral end plates (curved arrow). Notice the loss of normal contrast between the radiodensity of spinal column and adjacent soft tissues, reflecting reduced bore mass (porosis: porous bone).

Observed fracture rates were standardized against the US population rates for age, sex, and race (Table 1). One-sided Poisson probability test was used to determine the significance of the difference between observed and expected rates using a Bonferroni corrected standard. Poisson probability value of <.01 was considered statistically significant. For features with no national rates, relative risk was estimated by determining the odds ratio and 95% confidence limits. The odds ratio was considered significant at $P < .05$ if the 95% confidence bounds did not incorporate the number 1.[13]

Results

The Center's midstudy census was 994 residents. One or more fractures occurred among 114 (11.5%) residents. During 3.5 years, 182 bones were fractured, yielding a fracture rate of 5.2 fractures per 100 person-years (Table 1). The observed rate was 1.7 times greater than the fracture rate (3.0 fractures per 100 person-years) for the US population[2].

Fracture rates standardized for age, sex, and race are presented in Table 1. The observed number of fractures (n = 182) was significantly greater than the expected number of fractures (n = 104). The fracture rate was significantly greater in residents with epilepsy, male gender, older age, white race, osteoporosis, ambulation, and residence in intermediate-care-units. Rate was not affected by the severity of mental retardation (Table 2).

Fracture incidence stratified by the affected bone is presented in Table 3. Most fractures (n = 105 or 58%) occurred in hand (n = 62) and foot (n = 43) bones. Fracture incidence according to the number of fractures per affected subject is presented in Table 4; 87% of subjects sustained only one or two fractures. Causes of fractures are presented in Table 5; falls were related to 41 (23%) fractures. Features suggestive of osteoporosis (Figure 1) and osteomalacia (Figure 2) were present in occasional radiographic films.

Discussion

The fracture rate is significantly greater in our residents than the noninstitutionalized civilian US population (5.2 versus 3.0 fractures per 100 person-years, Table 1).[2] This is a cause for concern. Most civilians sustain fractures following significant trauma related to work, sports, or automobiles. In contrast, our residents are at minimal risk for such injury as they live in a sheltered environment. Fewer than 10% are employed (in low hazard occupations such as collating, sorting, assembling, and food serving). Sports are light, and involve minimal physical contact. Road trips are few, so no commute is involved.

It can be argued that the published fracture incidence for the US population is spuriously low due to poor case finding related to the use of interviews as the data source. This potential weakness is unlikely to be significant, since 97% of all fractures inevitably produce clinical manifestations leading to a definite diagnosis. Contrarily, the US rate may be spuriously high as its numerator, but not ours, includes dislocations in addition to fractures.[2]

TABLE 1.—*Observed Fractures Standardized for Age, Sex, and Race with US Population*

Feature, Number of Residents (n)	*Number of Fractures Observed/Expected in 3.5 y*	*Rate Observed/Expected per 100 Person-y*	*Poisson Probability One-sided Test*
Males, age			
<5 y, *n* = 3	0/0.1	0/1.5	N/A
5–17 y, *n* = 21	3/3.8	4.1/5.1	.72268
18–44 y, *n* = 458	91/64.1	5.7/4	.00090
>45 y, *n* = 97	20/8.2	5.9/2.4	.00032
Total, *n* = 579	114/76	5.6/3.6	.00001
Females, age			
<5 y, *n* = 2	0/.2	0/2.4	N/A
5–17 y, *n* = 21	1/3	1.4/4.1	.95088
18–44 y, *n* = 309	40/16.2	3.7/1.5	.00001
>45 y, *n* = 83	27/9	9.3/3.1	.00001
Total, *n* = 415	68/28	4.7/2.5	.00001
Race			
White, *n* = 771	165/89	6.1/3.3	.00001
Nonwhite, *n* = 223	17/17	2.2/2.2	.54864
Total, *n* = 994	182/104	5.2/3.0	.00001

Poisson probability: The difference between the observed rate and the expected rate is statistically significant if the value is less than .01, using a Bonferroni corrected standard of .0009 = .01/11.

N/A: Not Applicable. Sample size and/or number of observations are insufficient to test the hypothesis.

Calculation of observed fracture rate per 100 person years: Number of fractures in 3.5 years × 100 ÷ resident census ÷ 3.5 years.

TABLE 2.—*Epidemiologic Features of Study Population, Number of Bones Fractured, and Fracture Rates During 3.5 Years*

Feature	*Sample Size, n*	*Fractures: Number, Rate per 100 Person-y*	*Odds Ratio*	*95% Confidence Bounds*
Epilepsy			1.886	1.356–2.624
Present	295	75, 7.3		
Absent	699	107, 4.4		
Gender			2.088	1.337–3.261
Male	579	114, 5.6		
Female	415	68, 4.7		
Race			3.2999	2.002–5.438
White	771	165 6.1		
Nonwhite	223	17 2.2		
Osteoporosis			2.794	1.973–3.956
Present	196	64, 9.3		
Absent	798	118, 3.0		
Mobility			.329	.218–.497
Nonambulatory	317	28, 2.5		
Ambulatory	677	154, 6.5		
Care level			.426	.300–.607
Skilled nursing	412	47, 3.3		
Intermediate care	582	135, 6.6		
Mental retardation			.967	.662–1.413
Profound	764	139, 5.2		
Nonprofound	230	43, 5.3		

Odds ratio is an estimate of the relative risk. The observed difference is significant at $P < .05$ if the 95% confidence bounds do not incorporate the number 1.

Note: fracture rate for US population not available for these groups.

TABLE 3.—*Fracture Incidence According to the Affected Bone*

Bone name	*Number*	*%*
Skull	1	0.5
Vertebra	2	1.1
Nose	7	3.8
Face	3	1.6
Clavicle	4	2.2
Humerus	7	3.8
Radius	3	1.6
Ulna	3	1.6
Carpal bones	0	0
Metacarpal bones	19	10.4
Phalanx, hand	43	23.6
Rib	10	5.5
Sternum	0	0
Pelvis	0	0
Femur	13	7.1
Patella	1	0.5
Tibia	9	4.9
Fibula	11	6.0
Tarsal bones	3	1.6
Metatarsal bones	19	10.4
Phalanx, foot	24	13.2
Total fractures	182	100.0

TABLE 4.—*Frequency of Fractures per Resident During 3.5 Years*

Fractures per Resident	*Number of Residents*	*Total Fractures*
1	69	69
2	30	60
3	9	27
4	5	20
5	0	0
6	1	6
Grand total	114	182

TABLE 5.—*Fractures Stratified by their Causes*

Cause of Fracture	*Fractures*	*Number %*
Fall		
From wheelchair	4	2
From bed	3	2
Spontaneous/seizure	34	19
Assault by peer	5	3
Self-mutilation	11	6
Accident*	15	8
Care-related†	5	3
Unknown	105	58
Total	182	100

*Accidents: caught in door, 8; falling objects, 7.
†Care-related: transfers from bed to chair, therapeutic exercises.

Figure 2.—Radiograph illustrating osteomalacia. The two short bold arrows point to a healing fracture of the humerus with abundant callus formation (paired thin arrows). Curved arrow points to the prominent bone trabeculae. Note the delay in fusion of the proximal humeral epiphysis (two bold serrated arrows) with the shaft in this 33-year-old man; fusion usually is complete by the age of 18 years. Note the abnormal curvature of the humeral shaft reflecting bone softening (malacia).

The fracture rate was significantly higher among older residents (Table 1). This may indicate that the older residents represent a different cohort of subjects. The younger group has had lesser exposure to psychotropic medicines (20% in 1999 versus 60% in 1977), and has received more balanced nutrition (meeting US Recommended Daily Allowance, planned by licensed dietitians), and physical and occupational therapy. Higher fracture rate among the older residents may also reflect the combined effect of aging, immobilization-osteoporosis, and anticonvulsant-osteomalacia.

Of all residents, 295 (30%) had epilepsy requiring anticonvulsants. The fracture rate was higher among epileptics (Table 2), as observed previously.[3–9] This is probably due to fractures caused by violent muscle contractions, atonic falls, osteoporosis, and osteomalacia. Residents with drug-refractory seizures may develop immobilization-osteoporosis due to activity restrictions, imposed because financial constraints restrict the provision of one-on-one supervision.[14] Anticonvulsants (phenobarbital, carbamazepine, and phenytoin) may cause osteomalacia, as they induce liver microsomal enzymes

TABLE 6.—*Recommendations for Fracture Control at the Developmental Center*

I. Primary prevention: Reduce fracture incidence.

1. Host Factors: Interdisciplinary team should assess each resident's risk for fractures and develop a comprehensive customized fracture prevention plan. Consider history of prior fractures; risk for falls (seizure, prior fall, dizziness, cognitive impairment, postural hypotension, drug side effect, cardiac arrhythmia, impaired mobility); seizure (type, frequency, aura, prior injury); osteoporosis (immobility, age, calcium and estrogen supplement); and osteomalacia (sun exposure, vitamin D intake, anticonvulsants). Screen fracture-risk residents for osteoporosis by noninvasive dual energy x-ray absorptiometry,[20] or bone turnover markers (serum osteocalcin, urine n-telopeptide), and for osteomalacia by serum and/or urine levels of calcium, phosphorus, and 25-hydroxy vitamin D.
2. Enhanced bone strength: Maintain good nutrition. Prevent anticonvulsant-osteomalacia by calcium and vitamin D supplements and sunlight exposure. Offer physiotherapeutic and swimming exercises starting at an early age to maintain bone mass. Prevent and treat osteoporosis with alendronate,[21] and estrogen replacement therapy for females.
3. Adequate diagnosis and treatment of epilepsy: Preferential use of anticonvulsant monotherapy.
4. Personal protective devices: Facilitate normalization. Avoid custodial mentality. Use helmets and restraints as the last resort. Ensure proper helmet fit. Use a chin strap to prevent inadvertent removal by the resident or unintentional stripping during a fall. Use padded bed-rails for residents prone to a seizure or fall.
5. Injury prevention: Provide adequate staffing with trained and caring personnel. Provide individualized supervision through foster grandparents. Provide assistance during ambulation. Use proper lifting techniques and equipment for assisted transfers. Effectively manage residents with maladaptive behavior. Provide well-fitting footwear. Avoid loose shoe laces or excessively long pants. Develop good vocational programs. Provide more outdoor and recreational areas to keep residents occupied.
6. Safe Environment: Provide adequate illumination. Eliminate hazards (obstacles, throw rugs, floor wires, stray toys, wet or slippery floors). Repair doors that close abruptly to prevent fingers getting caught between door and the door jam. Install nonslip floorings, handrails. Fill gopher holes in ground. Use low beds for persons prone to fall from bed. Use shower chairs and padded pedestal baths as indicated. Provide separate accommodation for fracture-prone and blind residents away from wheelchair-users or those with maladaptive behavior. Avoid excessive noise and traffic in hallways. Evaluate resident density and space per person.
7. Wheelchair safety: Provide residents their usual wheelchairs. Install spoke covers for self-propelling residents, anti-tip devices, padded side rails, foot rests, etc.

II. Secondary prevention: Reduce fracture morbidity by early diagnosis and treatment.

1. High index of suspicion, careful physical examination, prudent use of radiographs.
2. Prompt and intensive treatment of all fractures.

III. Tertiary prevention: Reduce fracture-related morbidity.

1. Physical medicine and rehabilitation: Correction of deformities and use of orthotic devices to aid in ambulation.
2. Corrective orthopedic management of fracture malunions and nonunions.

to inactivate vitamin D and produce hypovitaminosis D, inhibit intestinal calcium transport, cause secondary hyperparathyroidism, and suppress osteoblasts.[15,16]

Inexplicably, the fracture rate was higher in the male gender. Higher fracture rate among white subjects probably reflects their greater predisposition to osteoporosis.[14] The fracture rate was not affected by the level of mental retardation.

The fracture rate was higher among residents with osteoporosis (Table 2). Persons of all ages, who present with fractures sustained from minimal trauma without other bone disease, probably have osteoporosis.[14,17,18] The cause of osteoporosis in our residents is probably prolonged immobilization related to severe neurologic-orthopedic disability.[14] This theory is corroborated by the fact that immobilization-osteoporosis leads to a balanced decrease in cortical and trabecular bone mass, and results in fractures involving all bones,[18] as noted in our study (Table 3). In contrast, the commoner postmenopausal osteoporosis predominantly affects vertebrae (trabecular bone).

The fracture rate was higher among ambulatory residents (Table 2). This is probably secondary to their increased physical activity, or falls (due to seizure, unsteady gait, drug side effects, maladaptive behavior, and orthopedic or neurologic disability). Probably for the same reasons, the fracture rate was higher among residents requiring intermediate care (usually ambulatory) than residents receiving skilled nursing care (who tend to be more disabled, sicker, or bedridden). The lower fracture rate in bedridden residents may be counter-intuitive, as recumbency would seem to predispose them to osteoporosis. This risk, however, may be offset by their reduced risk for injuries and superb handling by caring staff.

Femur fractures occurred in 13 subjects (7%) (Table 3). These are among the most clinically significant fractures, as they generally require surgical fixation and extended convalescence, and predispose patients to complications (eg, impaired ambulation, pneumonia, pressure ulcers, urinary tract infection, and reduced life span).[14]

Fractures of hand (n = 62) and foot (n = 43) bones accounted for 105 (58%) of the 182 fractures (Table 3). Although these small bone fractures usually require only conservative management, they can nonetheless considerably interfere with activities of daily living in persons with preexisting handicaps. Small bones are probably at a higher risk of injury because of greater interaction with the environment (for example, during opening or closing of doors), defense against injuries (bracing with hands

and feet to prevent a fall, or self-defense against assault), and relative underprotection against extraneous forces (due to their exposed location) compared to the trunk.

Vertebral fracture was recorded in only 2 cases (1.1%) (Table 3). Its low incidence is puzzling, as it is reportedly common in persons with epilepsy[19] or osteoporosis.[14] In this study, vertebral fracture was probably underdiagnosed due to the lack of a universally accepted radiological definition, difficulty in diagnosis in persons with coexisting severe spinal deformities, its frequent asymptomatic nature[14] (especially in bedridden nonverbal patients), and potential underdiagnosis due to the retrospective nature of our study.

Of the 114 subjects who sustained a fracture, 45 (40%) had a repeat fracture accounting for a total of 113 (62% of all) fractures (Table 4). This suggests that persons with a prior fracture are at an increased risk of future fractures. Predisposition to recurrent fractures was rather dramatic in a young man with epilepsy and osteoporosis who sustained a total of 18 fractures during 19 years.[9]

The cause of fracture was unknown in 105 cases (58%) (Table 5). Due to the severity of their mental retardation, many residents are unable to identify an injury or verbalize its effects. Many fractures cannot be diagnosed unless there is apparent deformity, bruise, impairment of motion, or refusal to use a part. Since many subjects are nonambulatory, fracture detection may be even more difficult. Since minor injuries (due to fall, assault, seizure, head banging, temper tantrum, or during transfer from bed to chair) are frequent, it may be difficult to attribute a given fracture to a specific injury. Most fractures of unknown cause were probably related to an unwitnessed seizure or fall.

Comparing our findings with two other studies of people with DD is instructive. In New England, during 10 months (June 1986–April 1987), 61 fractures occurred among 55 residents (rate: 13.2 fractures per 100 person-years).[3] This higher fracture rate may be because 98% of the subjects had epilepsy compared to only 30% in our study, and may also reflect better case finding in a prospective study. No vertebral fracture was recorded; 52% of fractures involved hand and foot bones. The femur was fractured in 6 cases (10%). The cause of fractures was known in 64% of cases (compared to 42% in our study); this greater knowledge may be related to the prospective nature of their study.

In our sister developmental center in Northern California, during 2 years (February 1995–January 1997), 104 fractures occurred among 961 residents (rate: 5.4 fractures per 100 person-years) (unpublished report; Fractures at Sonoma Developmental Center, 1995–1997; Iacovoni V, Jenkins D, Phillips S, May 1, 1997). No vertebral fracture occurred; 55% of the fractures involved hand and foot bones. The femur was fractured in 12 cases (12%). Fracture cause was known in only 30% of cases. These findings are similar to ours and reflect similarity of our two populations.

Our study suggests that fractures are an important cause of preventable morbidity in people with DD. It behooves their caretakers and physicians to exercise extra care not to let a fracture go undiagnosed. Pain, particularly post-seizure pain, should not be dismissed as a musculoligamentous injury until a fracture has been excluded radiographically. Diagnosis may be difficult due to lack of a history of significant trauma, difficulty in examining a person with severe contractures, and absence of additional functional impairment in an already nonambulatory nonverbal person.

In a nondisabled person, a fracture usually resolves with no permanent disability. In a disabled individual with marginal mental and physical reserves, however, it can produce additive, and at times, multiplicative permanent disability. The outcome may be devastating to that resident's independence, developmental programming, or activities of daily living. Although preventive health care is important for all, it can provide a much greater proportional return in people with DD. With major recent advances in the diagnosis and treatment of osteoporosis, a lot more can be done to control fractures than was possible a decade ago.[20,21] Steps recommended to prevent fractures at our center are listed in Table 6. Continued surveillance and follow-up studies are necessary to evaluate the effectiveness of these control measures.

Acknowledgments

The authors are profoundly grateful to Robert Newcomb, PhD (Professor of Statistics, University of California, Irvine, CA) for statistical consulting; Barbara Rycroft, MA, for literature search; Myra Rhodes for fracture data; Vernon Martinazzi, PhD, for pharmacy data; Terri Kipfstuhl for medical records; Joseph McKay, BS, for laboratory services; and Myron Dimmett, RN; Jerome Tobis, MD; Carl Weinert, MD; Nancy Greep, MD; and Thanh Phuong, MD; for advice.

REFERENCES

1. Department of Developmental Services, State of California. Consumer Handbook, January 1992 through December 1997. Sacramento CA 95814. May 1998, pp 1–25

2. Department of Health and Human Services. Vital and health statistics. Current estimates from the National Health Interview Survey 2994. Series 10: Data from the National Health Survey number 193. National Center for Health Statistics. DHHS Publication PHS 96-1521, 1995; pp 12–14

3. Tannenbaum T, Lipworth L, Baker S. Risk of fractures in an intermediate care facility for persons with mental retardation. Am J Ment Retard 1989; 93:444–451

4. Annegers J, Melton J, Sun C. Risk of age related fractures in patients with unprovoked seizures. Epilepsia 1989; 30:348–355

5. Murzic W, Taylor J, Bargar W. Seizure induced femur fracture after total hip replacement. Orthopedics 1993; 16:906–910

6. Vanderhooft E, Swiontkowski M. Bilateral femoral neck fractures following a grand mal seizure. Ann Emerg Med 1994; 24:1188–1191

7. Nakken K, Lossius R. Seizure related injuries in multihandicapped patients with therapy resistant epilepsy. Epilepsia 1993; 34:836–840

8. Nilsson O, Lindholm T, Elmstedt E. Fracture incidence and bone disease in epileptics receiving longterm anticonvulsant drug treatment. Arch Orthop Trauma Surg 1986; 105:146–149

9. Lohiya G, Lohiya S, Tan-Figueroa L. Eighteen fractures in a man with profound mental retardation. Ment Retard 1999; 37:47–51

10. Lohiya S, Lohiya G, Caires S. Hepatocellular carcinoma in hepatitis B surface antigen carriers in eight institutions. West J Med 1988; 148:426–429

11. Lakin K, Anderson L, Prouty R. State institution populations less than one third of 1977, residents older with more impairments. Ment Retard 1999; 37:85–86

12. Coffelt et al v California Department of Developmental Services et al. Superior Court of California, #916401 (January 1994)

13. Agresti A. An Introduction to Categorical Data Analysis. New York, NY, Wiley, 1996, pp 1–176

14. Osteoporosis: Review of evidence for prevention, diagnosis and treatment. Osteoporosis Int 1998; 8(suppl 4):S7–S80

15. Hunt P, Wuchen M, Handal N. Bone disease induced by anticonvulsant therapy and treatment with calcitriol. Am J Dis Child 1986;140:715–718

16. Rado J, Harris A. Metabolic bone disease, anticonvulsant osteomalacia and renal tubular acidosis in tuberous sclerosis. Intern Med 1993; 32:574–579

17. Seeman E. Osteoporosis in men: epidemiology, pathophysiology and treatment possibilities. Am J Med 1993; 95:22s–28s

18. Sepulveda D, Allison D, Gomez J. Low spinal and pelvic bone mineral densities among individuals with Down Syndrome. Am J Ment Retard 1995; 100:109–114

19. Kjaersgard P, Christianson C, Ahlgren P. Incidence of fractures of the vertebral spine in epileptic patients. Acta Neurol Scand 1976; 54:200–204

20. Kleerekoper M, Nelson D, Flynn M. Comparison of radiographic absorptiometry with dual energy X-ray absorptiometry. J Bone Miner Res 1994; 9:1745–1749

21. Cummings S, Black D, Thompson D. Effect of alendronate on risk of fracture. JAMA 1998; 280:2077–2082

Original Research

Type 2 Diabetes Mellitus in Navajo Adolescents

CATHERINE KIM, MD, MPH; CHRISTINA McHUGH, MD; YEONG KWOK, MD; APRIL SMITH, RD, CDE, MPH;
Crownpoint, New Mexico

Diabetes mellitus afflicts over one-fifth of the Navajo population aged over 20 years, but the prevalence of diabetes in Navajo adolescents is unclear. We conducted voluntary testing for diabetes mellitus at two high schools on the Navajo reservation to clarify the prevalence as well as to assess the utility of a high-school based screening program. Body mass index measurements (BMI), oral glucose tolerance tests, and hemoglobin A1C measurements were obtained in consenting high school students. Of the 276 students that participated, 234 were Navajo. Only one Navajo student (0.4%) had diabetes mellitus, although eight (3%) had impaired glucose tolerance or impaired fasting glucose. Participant BMI did not differ significantly from nonparticipant BMI. No correlation existed between BMI or impaired glucose handling, and significant overlap existed between the hemoglobin A1C values of students with impaired glucose handling and students without impaired glucose handling. Increased participation in screening programs may reveal higher disease prevalence, but high school–based screening is not justified by this study, despite the high rates of diabetes mellitus in the Navajo population.

(Kim C, McHugh C, Kwok Y, Smith A. Type 2 diabetes mellitus in Navajo adolescents. West J Med 1999; 170:210–213)

Type 2 diabetes mellitus, or non-insulin dependent diabetes mellitus, is a common chronic health problem among the Navajo tribe. According to the Navajo Health and Nutrition Survey (NHNS), a population-based reservation-wide study, type 2 diabetes afflicts 22.9% of Navajo aged 20 years and older. This is markedly higher than the age-standardized estimates for the general United States population.[1]

The link between obesity and type 2 diabetes mellitus in the Navajo has not been clarified; the degree and prevalence of obesity varies among different racial groups. While obesity is apparent in no more than 30% of Chinese and Japanese patients with type 2 diabetes mellitus, it is found in 75%–80% of North Americans, Europeans, or Africans with type 2 diabetes and approaches 100% of patients with type 2 among Pima Indians or Pacific Islanders from Nauru or Samoa.[2] Navajo adolescents have a 35%–40% prevalence of obesity and are roughly 2 kg/m^2 heavier than adolescents in the general United States population; therefore they may be at increased risk for diabetes.[3] In Navajo aged 12–19 years, the NHNS survey estimated a combined 8% prevalence of impaired glucose tolerance and diabetes mellitus, which is comparable to that seen among young and middle-aged adults in the general United States population. This age group, however, had a relatively small representation of 160 participants in the survey, and therefore it is possible that the survey could have underestimated the prevalence of diabetes.

Substantial evidence exists that improved glucose control in diabetes mellitus reduces the incidence of microvascular and perhaps macrovascular complications.[4,5] Theoretically, diagnosing diabetes mellitus earlier in its course could lead to earlier improved glucose control over a longer period of time.

In an attempt to further clarify the prevalence of diabetes mellitus in Navajo adolescents and to test the feasibility of a school screening program, we offered testing at two high schools on the Navajo reservation using the oral glucose tolerance test (OGTT).

Methods

Study Design

The target population was students aged 13–20 at two high schools on the Navajo reservation. Several weeks before screening, students and parents were informed of screening for diabetes through fliers and announcements at the high schools; participants were offered T-shirts, water bottles, gift certificates, food, and education. In order to participate, students, unless they were 18 years of age or older, had to submit an informed consent signed by their parents and themselves. Students were excluded if they

From the United States Public Health Service, Crownpoint Healthcare Facility, Crownpoint, New Mexico.
Reprint requests to Catherine Kim, MD, MPH, Robert Wood Johnson Clinical Scholars, H-220A Health Sciences Center, University of Washington, Seattle, WA 98195-7183 (e-mail: cathykim@worldnet.att.net).

TABLE 1.—*Body Mass Indices of Participants and Non-Participants by Age and Sex*

	Participants Median BMI (kg/m²)	*>95th percentile BMI*	*Non-Participants BMI (kg/m²)*	*>95th percentile BMI*	*P-value*
Age 13–14 y					
	8oys (*n* = 11) 22.96	(*n* = 4) 25.5	8oys (*n* = 23) 22.91	(*n* = 6) 25.5	0.796
	Girls (*n* = 23) 25.43	(*n* = 7) 27.0	Girls (*n* = 34) 22.32	(*n* = 5) 27.5	0.094
Age 15 y					
	Boys (*n* = 30) 25.04	(*n* = 9) 27.5	Boys (*n* = 30) 20.96	(*n* = 9) 27.5	0.326
	Girls (*n* = 50) 25.42	(*n* = 11) 28.5	Girls (*n* = 47) 24.11	(*n* = 8) 29.0	0.655
Age 16 y					
	Boys (*n* = 22) 22.92	(*n* = 4) 28.0	Boys (*n* = 43) 23.40	(*n* = 8) 28.0	0.624
	Girls (*n* = 43) 23.45	(*n* = 10) 29.0	Girls (*n* = 38) 24.37	(*n* = 10) 29.0	0.579
Age 17 y					
	8oys (*n* = 11) 25.90	(*n* = 5) 29.0	8oys (*n* = 41) 23.21	(*n* = 8) 29.0	0.178
	Girls (*n* = 33) 24.77	(*n* = 8) 29.0	Girls (*n* = 48) 26.13	(*n* = 16) 29.0	0.453
Ages 18–21 y					
	8oys (*n* = 18) 24.80	(*n* = 3) 30.0	Boys (*n* = 30) 25.28	(*n* = 8) 30.0	0.884
	Girls (*n* = 35) 24.39	(*n* = 5) 30.0	Girls (*n* = 38) 24.89	(*n* = 8) 30.0	0.503
Total		276	66	372	86

BMI = body mass index

were pregnant, reported a medical history of diabetes mellitus or impaired glucose tolerance, were not fasting, or were acutely ill on the day of screening. High school students with chronic disease are tracked through the Indian Health Service school-based clinic registry, and only one student in the high schools had a history of diabetes mellitus and was excluded from screening for this reason.

The OGTT was administered according to World Health Organization (WHO) criteria.[6] A fasting blood sample was drawn after which students drank a solution of 75 grams of glucose. A second blood sample was drawn 2 hours later. Venous samples were collected in gray-top vacutainer tubes containing sodium fluoride. According to the requirements of the Navajo Nation Health Research Board, fasting plasma glucose and 2-hour postprandial glucose analysis were performed at the laboratory of the Crownpoint Healthcare Facility and the hemoglobin A1C analysis was performed at a reference laboratory (Quest Clinical Laboratories, El Paso, Texas). While awaiting their second blood draw, students participated in four teaching sessions given by a nutritionist, a physical therapist, a physician, and a physician's assistant on healthy diet and exercise plans and the pathophysiology and sequelae of type 2 diabetes mellitus.

Students were diagnosed as having type 2 diabetes mellitus if they met the criteria set by the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus: fasting plasma glucose ≥7.0 mmol/liter (126 mg/dl) or 2-hour postprandial glucose ≥11.1 mmol/liter (200 mg/dl).[7] They were diagnosed with impaired glucose tolerance if their two-hour glucose was ≥7.8 mmol/liter (140 mg/dl) and <11.1 mmol/liter (200 mg/dl), and they were diagnosed with impaired fasting glucose if their fasting plasma glucose was ≥6.1 mmol/liter (110 mg/dl) and <7.0 mmol/liter (126 mg/dl).

Students' heights and weights were obtained from either the school record or the hospital record; all values were measured within the past year by either the school nurses or the hospital staff. For comparison, we obtained the heights and weights of the nonparticipants from the school record when available. The body mass index (BMI) was compared to the national averages adjusted for age and sex.[8] The ethnicity of the students was elicited by asking the students at the time of screening.

Subjects and their parents were informed of the results of their tests, and clinical care was arranged for subjects with newly diagnosed diabetes mellitus. Students diagnosed with impaired glucose tolerance or impaired fasting glucose were given monthly educational sessions with their parents by a nutritionist and physician, and were placed in the hospital's chronic disease registry for tracking purposes.

We used STATA (1997, College Station, Texas), a statistics software package, to perform statistical analysis.[9] Unless otherwise indicated, analyses were done separately in groups stratified by age and sex. Descriptive and bivariate associations were assessed by using the *t* test for continuous variables and the chi-square test for dichotomous variables. Continuous associations were assessed by using the Spearman's correlation test for continuous variables. A two-sided *P* value of 0.05 or less was considered significant for all statistical models.

Results

Body Mass Index

Of 970 eligible high school students, 276 participated in diabetes screening (Table 1). Of the participants, 234 were Navajo. The non-Navajo participants were

TABLE 2.—*Median Age and BMI of Students with Diabetes Mellitus and Impaired Glucose Tolerance**

	Age (y)	BMI (kg/m^2)	Fasting Plasma Glucose (mmol/liter)	Hemoglobin A1C (% of control)	2-hour Plasma Glucose (mmol/liter)
Impaired glucose handling (n = 8)	16.01 (15.0–19.6)	26.7 (21.6–35.8)	4.9 (3.8–6.4)	5.1 (4.4–5.2) 88 (69-116)†	8.1 (4.7–8.8) 146 (85–159)†
Diabetes mellitus (n = 2)	17.0 (15.5–18.5)	25.0 (24.8–25.3)	15.4 (13.8–17.0)	14.9 (14.3–15.5) 277 (248-306)†	25.7 (24.8–26.6) 462.5 (446–479)†
Participants	16.41 (12.6–20.3)	24.8 (15.8–48.5)	4.4 (2.6–5.9)	4.9 (4.1–5.6)	4.8 (2.0–8.8)
Normal glucose handling				79 (47–106)†	86 (37–159)†
Nonparticipants	16.81 (13.2–21.7)	23.5 (14.2–55.6)			

*Median values given. Numbers in parentheses indicate range of values; if no parentheses are present, only one value is available.
†Median values given in mg/dl.

primarily white (n = 29) or Hispanic (n = 7). Heights and weights were available on 372 nonparticipants and used for comparison; race was not available on the nonparticipants, although the majority were Navajo. A higher percentage of females were represented among the participants (67%) versus the nonparticipants (56%) (P = .004).

The BMIs as measured in kg/m^2 of the participants and nonparticipants by sex and age are presented in Table 1. Height and weight were not available for one participant. Twenty-four percent of participants were overweight as defined by having a BMI exceeding the 95th percentile for their sex and age; 23% of nonparticipants were overweight (Table 1).[8] After adjustment for age and sex, participants and nonparticipants did not have significantly different BMIs, and the participants who were non-Navajo did not have a significantly different BMI from participants who were Navajo.

Diabetes Prevalence

Ten students were found to have impaired glucose handling: either diabetes mellitus, impaired glucose tolerance, or impaired fasting glucose. One student diagnosed with diabetes mellitus was white; the nine other students were Navajo. Fasting blood glucose values, 2-hour glucose values, BMI, and hemoglobin A1C values for these students are listed in Table 2; for comparison, Table 2 also lists these values for students with normal glucose handling as well as the age and BMI of nonparticipants.

Hemoglobin A1C values were highly correlated with fasting blood glucose values (r = 0.885) and 2 hour glucose values (r = 0.811). However, significant overlap existed in the hemoglobin A1C values of students with abnormal fasting blood glucose or 2-hour glucose values and the hemoglobin A1C values of normals. When the children with diabetes mellitus were excluded, the hemoglobin A1C values were indistinguishable (P = 0.468). No significant correlation between impaired glucose tolerance, impaired fasting glucose, diabetes mellitus, and BMI was found.

Comment

The high prevalence of diabetes mellitus among Navajo Indians is of concern, as it is one of the largest tribes in the United States, with membership exceeding 200,000, and therefore diabetes consumes a significant amount of health care resources.[10]

Screening for diabetes mellitus with the glucose tolerance test automatically tests patients for both impaired glucose tolerance as well as diabetes mellitus. Evidence supporting early intervention in impaired glucose tolerance (IGT) is controversial; while progression to diabetes is high in Pima Indians,[11] prospective studies of interventions to prevent progression to frank diabetes in patients with IGT have produced conflicting results,[12–14] and there is little evidence of benefit in treating IGT itself.[15,16] For patients with type 2 diabetes mellitus, however, early intervention and improved glucose control can decrease end-organ damage.[4,5]

Screening for diabetes in youth, however, is problematic. The Navajo adolescents would appear to be at high risk given the rates of diabetes mellitus in older age groups, but the exact prevalence of diabetes mellitus remains unclear due to adolescents' small representation in the NHNS population-based survey.[3] In addition, population-based screening programs are difficult to conduct on a regular basis.

To try to address these issues, we offered screening at two reservation high schools in order to evaluate a large number of adolescent participants. We found two students had diabetes mellitus, one of whom was non-Navajo, and eight had glucose intolerance, a rate of impaired glucose handling that was lower than previously found in the population-based survey NHNS. Also, we did not find a correlation between BMI and impaired glucose handling.

As previously reported in the literature, the hemoglobin A1C values did not serve as a good screening tool for impaired glucose tolerance.[17–19] The A1C of students with normal glucose tolerance test values did not differ significantly from the hemoglobin A1C values of

students with abnormal glucose tolerance test values. In the two students with diabetes mellitus, the hemoglobin A1C was significantly elevated, but the number of students we found with diabetes is too low to determine the hemoglobin A1C's efficacy as a screening tool for diabetes mellitus. In order to evaluate the sensitivity of the A1C within ±5%, and assuming the prevalence of diabetes in the population is at least 5% and the sensitivity is 50%, we would need to test 8000 students. If we assumed the prevalence is 5% and the sensitivity is 90%, we would need to test 4000 students.

There may be several reasons for the difference between our study and the NHNS. Our population consisted of volunteers, girls being better represented than boys, and participants may have been more health conscious. Students who had a family history of diabetes may have been afraid to participate for fear of confirmation of the diagnosis of diabetes.

The BMIs of students who participated and students who did not participate were not significantly different, but we did not have height and weight measurements for the entire eligible student population, and the students whose height and weight were available may represent a healthier population than those who were not measured; this would minimize the differences in body mass indices between participants and nonparticipants. Of note, the percent of overweight students in each group, or the students who exceeded the 95th percentile BMI for age and sex, was sometimes as high as 30% (Table 1). Finally, the majority of our students were 15 or 16 years of age and presumably would be at lower risk than older students, who were underrepresented.

With increased participation in a diabetes screening program, it is possible that there would be more students identified with impaired glucose handling. In this study, the students were given multiple incentives including T-shirts, water bottles, and gift certificates, but possibly other incentives such as a financial reward would be more successful. The screening program was held in the late spring, and perhaps holding the program at a different time of year would increase participation, although other constraints on resources make this difficult. The program was conducted at a small rural health care facility and required diversion of physician, physical therapy, nursing, nutrition, and laboratory personnel to the high school; this would not be feasible during the busy winter months or late fall when school sports physicals need to be conducted. Finally, the OGTT is a cumbersome tool for assessing the presence of diabetes mellitus, and the development of a test that would not involve ingesting sugar and having blood drawn twice would probably improve participation.

Given the low rate of diabetes mellitus and the questionable value of addressing IGT, we conclude that a high-school based screening program with a similar structure to the one outlined in this paper does not appear justified at this time. If the problem of low participation of students could be successfully addressed, however, a screening program might yield higher rates of diabetes mellitus and impaired glucose tolerance.

REFERENCES

1. Will JC, Strauss KF, Mendlein JM, Ballew C, White LL, Peter DG. Diabetes mellitus among Navajo Indians: findings from the Navajo Health and Nutrition Survey. J Nutrition 1997; 127:2106S–2113S

2. Karam JH. Diabetes mellitus and hypoglycemia. In Tierney LM, McPhee SJ, Papadakis MA (Eds). Current Medical Diagnosis and Treatment. 38th ed. Stamford, CT, Appleton & Lange, 1999, pp 1118–1160

3. Freedman DS, Serdula MK, Percy CA, Ballew C, White L. Obesity, levels of lipids and glucose, and smoking among Navajo adolescents. J Nutrition 1997; 127:2120S–2127S

4. Vijan S, Hofer TP, Hayward RA. Estimated benefits of glycemic control in microvascular complications in type 2 diabetes. Ann Intern Med 1997; 127:788–795

5. The relationship of glycemic exposure (HbA1c) to the risk of development and progression of retinopathy in the Diabetes Control and Complication Trial. Diabetes 1995; 44:968–983

6. World Health Organization. Diabetes mellitus. Report of a WHO Study Group. Geneva, World Health Org Tech Rep Ser, no. 727, 1985

7. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the Expert Committee on the diagnosis and classification of diabetes mellitus. Diabetes Care 1997; 20:1183–1197

8. Anthropometric reference data and prevalence of overweight, United States, 1976–1980. Vital and Health Statistics Series. Baltimore, MD, National Center for Health Statistics No. (PHS) 87-1688,1987

9. Stata Statistical Software. College Station, TX, Stata Corporation, 1997

10. Navajo Nation FAX 1993. Window Rock, AZ, Division of Economic Development, Navajo Nation, 1994

11. Saad MF, Knowler WC, Pettitt DJ, Nelson RG, Mott DM, Bennett PH. The natural history of the impaired glucose tolerance in the Pima Indians. N Engl J Med 1988; 319:1500–1506

12. Sartor G, Shersten B, Carlstrom S, Melander A, Norden A, Persson G. Ten-year follow-up of subjects with impaired glucose tolerance: prevention of diabetes by tolbutamide and diet regulation. Diabetes 1980; 29:41–49

13. Eriksson KF, Lindgarde F. Prevention of type 2 (non-insulin-dependent) diabetes mellitus by diet and physical exercise. The 6-year Malmo feasibility study. Diabetologia 1981; 34:391–398

14. Keen H, Jarrett RJ, McCartney P. The ten-year follow-up of the Bedford survey (1962–1972) glucose tolerance and diabetes. Diabetologia 1982; 22:73–78

15. Jarrett RJ, Keen H, McCartney P. The Whitehall Study; ten year follow-up report on men with impaired glucose tolerance with reference to worsening of diabetes and predictors of death. Diabetic Med 1984; 1:279–283

16. Genuth SM, Houser HB, Carter JR, et al. Observations on the value of mass indiscriminate screening for diabetes mellitus based on a five-year follow-up. Diabetes 1978; 27:377–383

17. Little RR, England JD, Wiedmeyer H, McKenzie EM, Pettitt DJ, Knowler WC, et al. Relationship of glycosylated hemoglobin to oral glucose tolerance. Diabetes 1988; 37:60–64

18. Modan M, Harris MI. Fasting plasma glucose in screening for NIDDM in the US and Israel. Diabetes Care 1994;17:436–439

19. Guillausseu PJ, Charles MA, Paolaggi F, Timsit J, Chanson P, Peynet J, et al. Comparison of HbA1 and fructosamine in diagnosis of glucose-tolerance abnormalities. Diabetes Care 1990; 13:898–900

Articles

Methamphetamine and the Expanding Complications of Amphetamines

TIMOTHY E. ALBERTSON, MD, PHD; ROBERT W. DERLET, MD;
BRENT E. VAN HOOZEN, MD; *Sacramento, California*

During the past 10 years, the use of methamphetamine has increased rapidly in the West and throughout the United States. Because of this increase, our attention has focused on methamphetamine's toxicity. Methamphetamine and related compounds generate many of the same toxic effects as cocaine. Because of methamphetamine's widespread use, clinicians should be familiar with its medical effects and toxicity and with treatment options for acute and long-term effects of methamphetamine abuse.

(Albertson TE, Derlet RW, Van Hoozen BE. Methamphetamine and the expanding complications of amphetamines. West J Med 1999; 170:214–219)

The use of methamphetamine hydrochloride (MAP) has increased markedly over the past 25 years. In San Diego County, California, MAP intoxication played a role in 40% of drug-related homicides in 1987, and 40% of drug rehabilitation referrals were related to MAP.[1] Maternal deaths associated with the use of MAP have also been reported.[2,3] A study of 29,494 women giving birth in California found that MAPs were the third most common illicit drugs found on toxicology screens (0.60%).[4] In San Bernardino County, twice as many more coroners' cases involved MAP than involved cocaine from 1980 to 1988.[5] Initially, MAP use was concentrated on the West Coast and in Hawaii, but later spread throughout the country.[5,6] A 1996 Drug Enforcement Administration report found large increases in MAP use in the West: For example, Phoenix reported a 570% increase in deaths related to MAP between 1992 and 1994.[7] Increases in use were also reported in the Southeast and Midwest. The increasing morbidity and mortality associated with MAP abuse are of great concern.[8,9]

Both oral and intravenous uses of MAP are well documented; but, until recently, the use of smokable MAP has received little attention in medical literature. Patients who inhale the smokable form of MAP ("ice") experience an immediate euphoria similar to that seen with "crack" cocaine, but the effects may last much longer than those seen with cocaine.[10] The immediate high that MAP provides, coupled with the drug's availability and low cost, may explain its popularity among adolescents.[11] A 1994 drug abuse survey found that the groups with the highest use of MAP were males aged 18 to 25 and females aged 12 to 17.[12]

Methamphetamine hydrochloride is relatively easy to synthesize; illicit production occurs in home kitchens, trailers, recreational vehicles, and rural cabins.[13] Once converted to its water-soluble form, MAP salt is sold on the street as "speed," "crank," "go," "crystal," or methamphetamine. Smoking MAP powder, crystals, or "ice" is done by placing the substance in a bowl-shaped piece of metal foil, a molded glass pipe, or a modified light bulb and heating it over the flame of a cigarette lighter or torch. The volatile MAP fumes are inhaled through a straw or pipe.

Street MAP may be mixed with many drugs including cocaine. Eight percent to 20% of street-available stimulants contain both MAP and cocaine.[14] In a report on cocaine intoxication, 7% of patients sought medical help resulting from the concurrent use of cocaine and amphetamines.[15]

Deaths related to amphetamines have been associated with assaults, suicides, homicides, accidents, driving impairment, and maternal-fetal and infant exposures.[1,2,16–19] In a recent study of drug abuse and alcohol consumption related to motor vehicle accidents in Belgium, MAP was the most commonly found drug other than alcohol.[20]

Causes of maternal deaths associated with amphetamine use include intracerebral hemorrhage, cardiovascular collapse, seizures, and amniotic fluid embolism.[3]

From the Division of Pulmonary and Critical Care Medicine, University of California, Davis, Medical Center, Sacramento, California, (Drs, Albertson and Van Hoozen); Division of Emergency Medicine and Clinical Toxicology (Drs Albertson and Derlet); Section of Pulmonary Medicine, Veterans Administration Northern California Health Care System Mather, Sacramento, California (Drs, Albertson and Van Hoozen); Sacramento Division, California Poison Control Center, Sacramento, California (Dr Albertson).

Reprint requests to Timothy E. Albertson, MD, PhD, Professor and Chief, Division of Pulmonary and Critical Care Medicine, University of California, Davis, Medical Center, 4150 V Street, Suite 3400, Sacramento, CA 95817 (e-mail: tealbertson@ucdavis.edu).

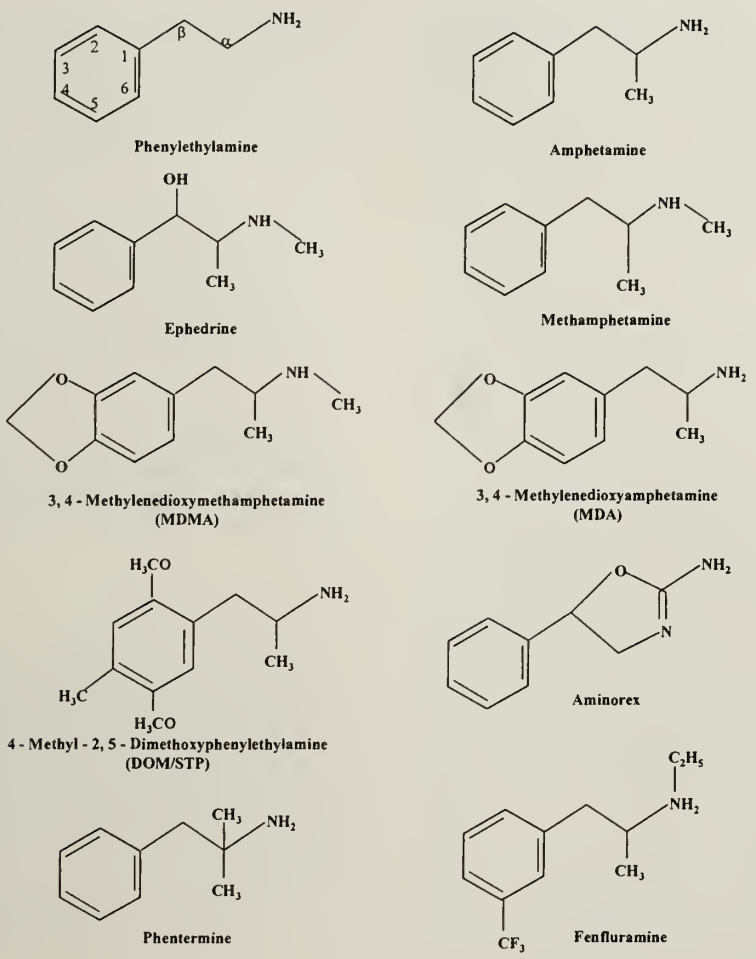


Figure 1.—The chemical structures of several amphetamine-like compounds are shown. The basic phenylethylamine structure is labeled. Both α and β side chain positions and the phenyl ring itself can be modified to alter the pharmacologic effects of these related compounds.

Increased risk for fetal and infant death is associated with maternal use of amphetamines.[2]

Clinical Pharmacology of Amphetamines

Amphetamines cause central nervous system (CNS) stimulation that may induce euphoria, increase alertness, intensify emotions, increase aggression, alter self-esteem, and allegedly increase sexuality.[21] Presynaptic reuptake of catecholamines—including dopamine, norepinephrine, and serotonin—is blocked, causing hyperstimulation at selected postsynaptic neuron receptors.[21–25] Indirectly, these hyperstimulated neurons can stimulate various other noncatecholamine CNS and peripheral pathways. Changes in mood, excitation level, motor movement, and appetite appear to be more directly mediated by central dopaminergic alterations.[22] Serotonin alterations may also contribute to the amphetamine-related mood changes, psychotic behavior, and aggressiveness.[21,22,25]

The half-life of amphetamines in humans ranges from 10 to 30 hours depending on the drug, urine pH, and dosage.[26,27] Methamphetamine hydrochloride has greater CNS effects compared to D-amphetamine, presumably because of prolonged half-life and increased CNS penetration.[28] A portion of MAP is metabolized to form amphetamine. The amphetamines are weak bases with pK_a values ranging from 8.8 to 10.4, and they are easily absorbed through the gut, airway, nasopharynx, muscle, placenta, and vagina.[25,29] Peak plasma levels are seen about 30 minutes after intravenous or intramuscular injection routes and about 2 to 3 hours after oral ingestion. Metabolism of amphetamines usually includes aromatic hydroxylation, aliphatic hydroxylation, and n-dealkylation, which give rise to both inactive and active metabolites such as the potent hallucinogen, p-hydroxyamphetamine [25](Fig. 1).

When MAP is used with ethanol, increased psychological and cardiac effects are seen.[30] Similarly,

TABLE 1.—*Major Signs and Symptoms of Amphetamine Toxicity*

Cardiac	
Chest Pain	+++
Myocardial infarction	+
Palpitations	++
Arrhythmia	++
Cardiomyopathy	+
Myocarditis	+
Hypertension	++
Sudden death	+
Valve thickening	+++
Neurologic	
Headache	+
Seizure	++
Cerebral infarcts/stroke	++
Cerebral vasculitis	++
Cerebral edema	+
Mydriasis	++
Cerebral hemorrhage	++
Subarachnoid	++
Intraventricular	+++
Intracerebral	++
Psychiatric	
Anxiety	+++
Depression	++
Paranoia	++
Delirium/hallucination	+++
Psychosis	+++
Suicide	++
Aggressive behavior	++
Euphoria/hyperactivity	++
Irritability	++
Respiratory	
Pulmonary edema	+
Dyspnea	++
Bronchitis	+
Pulmonary hypertension	+++
Hemoptysis	+
Pleuritic chest pain	++
Asthma exacerbation	+
Pulmonary granuloma	+
Other	
Ulcers	++
Hyperpyrexia	++
Renal failure	+
Ischemic colitis	+
Obstetric complications	++
Anorexia/weight loss	+++
Rhabdomyolysis	++
Nausea/vomiting	+
Disseminated vasculitis	+

Estimated frequency of events: +, reported rare cases; ++, commonly reported; +++, frequently seen or reported with chronic use or overdose.

simultaneous use of opioids and amphetamines, so-called "speedballing," increases toxicity.[29]

Because of the variability in quality and concentration of illicitly purchased MAP, the clinical observation of toxic effects is usually more relevant than an estimate of total ingested dose. Fatalities have been reported after ingestions as low as 105 mg per kg of MAP.[31] Blood levels of amphetamine in fatal cases have ranged from 0.5–41 mg/liter with an average of 8.6 mg/liter in a summary of 11 cases.[29] In addition, tachyphylaxis occurs with acute MAP use. Long-term users of amphetamine appear to tolerate higher doses (eg, averaging up to or greater than 1000 mg/d) with fewer symptoms.[28]

Clinical Toxicity

The acute and chronic toxic manifestations of MAP mimic those of all amphetamine-related compounds. Table 1 outlines the major signs and symptoms of MAP toxicity.

Cardiovascular System

Cardiovascular symptoms, including chest pain, palpitations, and dyspnea, are common.[32–34] The concern that thrombus formation may play a role in MAP-related myocardial infarctions has generated at least one case report of the use of a thorombolytic agent in addition to the use of nitrates and analgesics in treating these patients.[34] Significant hypotension with bradycardia and a metabolic acidosis has been seen in massive amphetamine overdoses.

Acute and chronic cardiomyopathy from MAP abuse is thought to be secondary to both direct amphetamine cardiac toxicity and indirect amphetamine-induced hypertension, necrosis, and ischemia.[35–38] Most reports of cardiomyopathy have been with oral and intravenous amphetamines, but cardiomyopathy has also been seen after smoking MAP.[39] Necrotizing angiitis with arterial aneurysms and sacculations has been seen in the kidney, liver, pancreas, and small bowel in MAP drug abusers.[40] Similarly, acute aortic dissections and arterial aneurysms have been associated with MAP abuse.[41]

Central Nervous System

In toxic doses, MAP induces unpleasant CNS symptoms such as agitation, anxiety, hallucinations, delirium, psychosis, seizures, and death.[31,42–44] Many patients who have used MAP present unconscious to an emergency department. In some of these persons, lack of responsiveness may be due in part to the use of other drugs such as opioids. Other patients may be unresponsive because of the direct effects of intravenous MAP use or the secondary effects of amphetamine induced seizures.[45] Other CNS disorders induced by amphetamines include cerebrovascular accidents due to hemorrhage or vasospasm, cerebral edema, and cerebral vasculitis.[46,47]

The initial feeling of physically and mentally enhanced powers following MAP use can quickly deteriorate with high doses or chronic use, resulting in

emotional lability, confusion, paranoia, and hallucinations.[48] In addition to the acute paranoid delusional psychosis associated with high-dose amphetamine use, a lasting psychosis similar to schizophrenia may be simply a persistent drug-induced psychosis or may represent the emergence of an underlying psychiatric disorder.[49]

Acute and chronic amphetamine exposures have also been associated with choreoathetoid movement disorders independent of Huntington's disease.[50,51] Amphetamine-induced seizures have been seen as isolated events or associated with hyperthermia, coma, muscle hyperactivity, metabolic acidosis, secondary rhabdomyolysis, renal failure, or shock.[6,45,52–54] Cerebral hemorrhage with arteriovenous malformations and with amphetamine-induced cerebral vasculitis has been reported in patients using amphetamines.[44,47,55–57] Cerebral artery spasm and occlusion leading to ischemic strokes and transient cortical blindness have been noted after MAP use.[58,59]

Infectious Diseases

Infectious disease is a risk associated with intravenous MAP use. An association has been seen between MAP use and the risk of endocarditis, viral hepatitis, and human immunodeficiency virus (HIV) disease.[11,60–62] High-risk sexual activity, including survival sex and homosexual/bisexual lifestyles, is associated with MAP use in adults and "street" youths.[11,62] In related findings, both increases and decreases in sexual desire and activity have been reported with amphetamine use, although increases are more common than decreases.[63]

Respiratory System

Like cocaine abusers, many amphetamine abuse patients present to emergency departments with respiratory symptoms.[6,64] Although the exact incidence and prevalence of amphetamine-induced pulmonary symptoms have not been reported, the variability of symptoms appears to depend on the amphetamine compound used, the dosage, and the route. Acute noncardiogenic pulmonary edema has been related to MAP use.

Pulmonary hypertension has long been reported in amphetamine users. In the late 1960s, users of intravenous, nasal inhalant, or oral street amphetamines were reported to have pulmonary artery muscular hypertrophy with foreign body granulomas consistent with significant pulmonary hypertension.[65–67] Contaminants have also been suggested as the cause of pulmonary hypertension associated with inhalation of MAP, although a direct role of MAP inhalation has not been eliminated.[68]

Systemic and Dermatologic Toxicity

Reports of amphetamines and amphetamine-related agents producing severe systemic toxicity are common. Presentation of systemic toxicity varies but may include pulmonary and cardiovascular manifestations in addition to fulminant hyperthermia, convulsions, rhabdomyolysis, acute renal failure, hepatocellular damage, disseminated intravascular coagulation, and refractory hypotension.[54,69] Renal failure associated with amphetamines has been related to hyperexia, rhabdomyolysis, and cardiovascular shock leading to acute tubular necrosis and necrotizing angiitis.[69–74] The renal necrotizing angiitis noted in some cases of renal failure has been seen in the presence of hepatitis B serum antigen, usually in intravenous abusers of amphetamines.[74] Amphetamine-induced acute interstitial nephritis was thought to be the cause of renal failure in one case report.[74]

Hepatocellular damage has been reported after both acute and chronic amphetamine abuse.[52,75,76] Direct toxic effects, hypotension, hepatotoxic contaminants, hepatic vasoconstriction, lipid peroxidation, occult viral causes, and necrotizing angiitis have been postulated as mechanisms for the amphetamine-induced hepatocellular toxicity.[76] Abuse of MAP has also been associated with the formation of giant gastrointestinal ulcers and ischemic colitis.[76,77] Of note, the presenting complaint of abdominal pain was seen in 4% of amphetamine toxic patients in one emergency department series.[6]

Although not formally studied, the most common dermatological manifestations in patients abusing amphetamine-related compounds are probably induced by trauma (including self-inflicted), intravenous needles, or burns.[79] A case of lichenoid drug eruption has been reported with the use of MAP.[80]

Treatment Approaches to Amphetamine Toxicity

Most cases of MAP toxicity can be managed supportively. Like all severe overdoses, MAP overdose requires immediate supportive care including airway control, oxygenation and ventilation support, and appropriate monitoring. In one study, as few as 10% of the patients presenting to emergency departments with amphetamine-related complaints required admission, and those who were admitted to the hospital were generally discharged within two days.[6] In severe overdoses, termination of amphetamine-induced seizure activity and arrhythmia is of immediate importance. Correction of hypertension, hypotension, hyperthermia, and metabolic and electrolyte abnormalities along with control of severe psychiatric agitation are indicated. Health maintenance activities, such as testing for hepatitis and HIV disease, should be considered.

Despite the ability of MAP to cause significant CNS and psychiatric activation, relatively few patients who present to emergency departments for acute intoxication require pharmacologic intervention.[6] In many emergency departments, patients can be treated for mild agitation with decreased stimuli alone unless they are thought to be a harm to themselves. The more severely hyperactive or agitated persons can be treated with an antipsychotic drug or a benzodiazepine.

Antipsychotic drugs that may specifically antagonize the central behavioral effects of MAP are haloperidol

and droperidol. Several clinical reports describe the efficacy of droperidol and haloperidol in acute amphetamine toxicity.[6,81] In a recent study of 146 patients presenting to the emergency department in an agitated, violent, or psychotic state from MAP, droperidol produced more rapid and profound sedation than lorazepam.[82] Haloperidol may quickly improve symptoms of patients with acute choreoathetoid syndrome associated with amphetamines. Benzodiazepines, such as diazepam (Valium), are used to terminate amphetamine-induced seizures.[82]

If sedation fails, several antihypertensive agents including β-blockers are effective in reversing MAP-induced cardiovascular symptoms. Earlier recommendations to acidify the urine to increase clearance were based on a single case report and are not recommended based on the risk for systemic acidification and exacerbation of potential rhabdomyolysis.[83] Rhabdomyolysis should be suspected and ruled out by drawing initial creatinine phosphokinase levels in any patient who presents to the emergency department in a severe, agitated state from amphetamines. Patients with rhabdomyolysis should be aggressively treated with fluids and admitted to the hospital. Renal function and vital signs, as well as fluid intake and output, should be monitored closely. Early and aggressive treatment of potential rhabdomyolysis is felt to improve the clinical outcome and decrease potential nephrotoxicity. Although we have focused on acute care, significant social and psychiatric intervention is needed to reduce the chance of long-term dependence on amphetamines.

Summary

Methamphetamine hydrochloride is an amphetamine with a high potential for abuse. Like other amphetamines, MAP can induce symptoms similar to euphoria. As a drug of abuse, MAP vies with cocaine in its appeal for long-term or recreational users wanting a rapid high through inhalation. The half-life of MAP may produce exceptionally long-lasting toxic effects. The possibility of amphetamine use or abuse should be considered in any patient presenting with psychosis, violence, seizures, rhabdomyolysis, trauma, or cardiovascular abnormalities.

REFERENCES

1. Bailey DN, Shaw RF. Cocaine- and methamphetamine-related deaths in San Diego County (1987): homicides and accidental overdoses. J Forensic Sci 1989; 34:407–22

2. Stewart JL, Meeker JE. Fetal and infant deaths associated with maternal methamphetamine abuse. J Anal Toxicol 1997; 21:515–517

3. Catanzarite VA, Stein DA. "Crystal" and pregnancy—methamphetamine-associated maternal deaths. West J Med 1995; 162:454–457

4. Vega WA, Kolody B, Hwang J, Noble A. Prevalence and magnitude of perinatal substance exposures in California. N Engl J Med 1993; 329:850–854

5. Puder KS, Kagan DV, Morgan JP. Illicit methamphetamine: analysis, synthesis, and availability [published erratum appears in Am J Drug Alcohol Abuse 1989; 15:353]. Am J Drug Alcohol Abuse 1988; 14:463–473

6. Derlet RW, Rice P, Horowitz BZ, Lord RV. Amphetamine toxicity: experience with 127 cases. J Emerg Med 1989; 7:157–161

7. National Conference of Federal, State, and Local Law Enforcement on Methamphetamine Regional Trends. Washington, DC, US Department of Justice, Drug Enforcement Administration, 1996, pp 7–8

8. National Institute on Drug Abuse Statistical Series Annual Data 1988. Rockville, Md, US Department of Health and Human Services (Public Health Service), National Institute on Drug Abuse, Division of Epidemiology and Prevention Research, 1989, Series 1, No 8

9. Centers for Disease Control and Prevention. Increasing morbidity and mortality associated with abuse of methamphetamine—United States, 1991–1994. MMWR Morb Mortal Wkly Rep 1995; 44:882–886

10. Jackson JG. The hazards of smokable methamphetamine [letter]. N Engl J Med 1989; 321:907

11. Kipke MD, O'Connor S, Palmer R, MacKenzie RG. Street youth in Los Angeles. Profile of a group at high risk for human immunodeficiency virus infection. Arch Pediatr Adolesc Med 1995; 149:513–519

12. Substance Abuse and Mental Health Services Administration. National Household Survey on Drug Abuse: Population Estimates 1994. Rockville, MD, US Department of Health and Human Services (Public Health Service), 1995, pp 61–65

13. Allen A, Cantrell T. Synthetic reductions in clandestine amphetamine and methamphetamine labs. J Forensic Sci 1989; 42:183–199

14. Klatt EC, Montgomery S, Namiki T, Noguchi TT. Misrepresentation of stimulant street drugs: a decade of experience in an analysis program. J Toxicol Clin Toxicol 1986; 24:441–450

15. Derlet RW, Albertson TE. Emergency department presentation of cocaine intoxication. Ann Emerg Med 1989; 18:182–186

16. Ellinwood EH Jr. Assault and homicide associated with amphetamine abuse. Am J Psychiatry 1971; 127:1170–1175

17. Kalant H, Kalant OJ. Death in amphetamine users: causes and rates. Can Med Assoc J 1975; 112:299–304

18. Logan BK. Methamphetamine and driving impairment. J Forensic Sci 1996; 41:457–464

19. Katsumata S, Sato K, Kashiwade H, et al. Sudden death due presumably to internal use of methamphetamine. Forensic Sci Int 1993; 62:209–215

20. Schepens PJ, Pauwels A, Van Damme P, Musuku A, Beaucourt L, Selala MI. Drugs of abuse and alcohol in weekend drivers involved in car crashes in Belgium. Ann Emerg Med 1998; 31:633–637

21. Gawin FH, Ellinwood EH Jr. Cocaine and other stimulants. actions, abuse, and treatment. N Engl J Med 1988; 318:1173–1182

22. Cho AK. Ice: a new dosage form of an old drug. Science 1990; 249:631–634

23. Pitts DK, Marwah J. Cocaine and central monoaminergic neurotransmission: a review of electrophysiological studies and comparison to amphetamine and antidepressants. Life Sci 1988; 42:949–968

24. Scheel-Kreuger J. Behavioural and biochemical comparison of amphetamine derivatives, cocaine, benztropine and tricyclic anti-depressant drugs. Eur J Pharmacol 1972; 18:63–73

25. Linden CH, Kulig KW, Rumack BH. Amphetamines. Top Emerg Med 1985; 7:18–32

26. Bryson PD. Comprehensive Review in Toxicology. Rockville, MD, Aspen Publications, 1989, pp 370–372

27. Beckett AH, Rowland M. Urinary excretion kinetics of amphetamine in man. J Pharm Pharmacol 1965; 17:628–639

28. Lake C, Quirk R. CNS stimulants and the look-alike drugs. Psychiatr Clin North Am 1984; 7:689–701

29. Baselt RC, Cravey RH. Amphetamine. Disposition of Toxic Drugs and Chemicals in Man. Foster City, Calif, Chemical Toxicology Institute, 1995, pp 44–47

30. Mendelson J, Jones RT, Upton R, Jacob P III. Methamphetamine and ethanol interactions in humans. Clin Pharm Ther 1995; 57:559–568

31. Kramer JC, Fischman VS, Littlefield DC. Amphetamine abuse. pattern and effects of high doses taken intravenously. JAMA 1967; 201:305–309

32. Lam D, Goldschlager N. Myocardial injury associated with polysubstance abuse. Am Heart J 1988; 115:675–680

33. Bashour TT. Acute myocardial infarction resulting from amphetamine abuse: a spasm-thrombus interplay? Am Heart J 1994; 128:1237–1239

34. Furst SR, Fallon SP, Reznik GN, Shah PK. Myocardial infarction after inhalation of methamphetamine [letter]. N Engl J Med 1990; 323:1147–1148

35. Call TD, Hartneck J, Dickinson WA, Hartman CW, Bartel AG. Acute cardiomyopathy secondary to intravenous amphetamine abuse. Ann Intern Med 1982; 97:559–560

36. Croft CH, Firth BG, Hillis LD. Propylhexedrine-induced left ventricular dysfunction. Ann Intern Med 1982; 97:560–561

37. Smith HJ, Roche AH, Jausch MF, Herdson PB. Cardiomyopathy associated with amphetamine administration. Am Heart J 1976; 91:792–797

38. O'Neill ME, Arnolda LF, Coles DM, Nikolic G. Acute amphetamine cardiomyopathy in a drug addict. Clin Cardiol 1983; 6:189–191

39. Hong R, Matsuyama E, Nur K. Cardiomyopathy associated with the smoking of crystal methamphetamine. JAMA 1991; 265:1152–1154

40. Citron BP, Halpern M, McCarron M, et al. Necrotizing angiitis associated with drug abuse. N Engl J Med 1970; 283:1003–1011

41. Davis GG, Swalwell CI. Acute aortic dissections and ruptured berry aneurysms associated with methamphetamine abuse. J Forensic Sci 1994; 39:1481–1485

42. Wilson JM, Kalsinksy KS, Levey AL, et al. Striatal dopamine nerve terminal markers in human chronic methamphetamine users. Nature Med 1996; 2:699–703

43. Zalis EG, Parmley LF. Fatal Amphetamine Poisoning. Arch Intern Med 1963; 101:822–826

44. Conci F, D'Angelo V, Tampieri D, Vecchi G. Intracerebral hemorrhage and angiographic beading following amphetamine abuse. Ital J Neurol Sci 1988; 9:77–81

45. Hall AP, Lyburn ID, Spears FD, Riley B. An unusual case of ecstasy poisoning. Intensive Care Med 1996; 22:670–671

46. Chynn KY. Acute subarachnoid hemorrhage. JAMA 1975; 233:55–56

47. Salanova V, Taubner R. Intracerebral haemorrhage and vasculitis secondary to amphetamine use. Postgrad Med J 1984; 60:429–430

48. Smith DE, Fischer CM. An analysis of 310 cases of acute high-dose methamphetamine toxicity in Haight-Ashbury. Clin Toxicol 1970; 3:117–124

49. Sato M. A lasting vulnerability to psychosis in patients with previous methamphetamine psychosis. Ann NY Acad Sci 1992; 654:160–170

50. Rhee KJ, Albertson TE, Douglas JC. Choreoathetoid disorder associated with amphetamine-like drugs. Am J Emerg Med 1988; 6:131–133

51. Lundh H, Tunving K. An extrapyramidal choreiform syndrome caused by amphetamine addiction. J Neurol Neurosurg Psychiatry 1981; 44:728–730

52. Henry JA, Jeffreys KJ, Dawling S. Toxicity and deaths from 3,4-methylenedioxymethamphetamine ("ecstasy"). Lancet 1992; 340:384–387

53. Simpson DL, Rumack BH. Methylenedioxymethamphetamine clinical description of overdose, death, and review of pharmacology. Arch Intern Med 1981; 141:1507–1509

54. Chan P, Chen JH, Lee MH, Deng JF. Fatal and nonfatal methamphetamine intoxication in the intensive care unit. J Toxicol Clin Toxicol 1994; 32:147–155

55. Lukes SA. Intracerebral hemorrhage from an arteriovenous malformation after amphetamine injection. Arch Neurol 1983; 40:60–61

56. Matick H, Anderson D, Brumlik J. Cerebral vasculitis associated with oral amphetamine overdose. Arch Neurol 1983; 40:253–254

57. Hughes JC, McCabe M, Evans RJ. Intracranial haemorrhage associated with ingestion of "ecstasy". Arch Emerg Med 1993; 10:372–374

58. Rothrock JF, Rubenstein R, Lyden PD. Ischemic stroke associated with methamphetamine inhalation. Neurol 1988; 38:589–592

59. Gospe SM Jr. Transient cortical blindness in an infant exposed to methamphetamine. Ann Emerg Med 1995; 26:380–382

60. Molitor F, Truax SR, Ruiz JD, Sun RK. Association of methamphetamine use during sex with risky sexual behaviors and HIV infection among non-injection drug users. West J Med 1998; 168:93–97

61. Anderson R, Flynn N. The methamphetamine–HIV connection in Northern California. In Klee H (Ed). Amphetamine Misuse: International Perspectives on Current Trends, The Netherlands, Harwood Academic Publishers, 1997, pp 181–196

62. Gorman EM, Morgan P, Lambert EY. Qualitative research considerations and other issues in the study of methamphetamine use among men who have sex with other men. NIDA Res Monogr 1995; 157:156–181

63. Meston CM, Gorzalka BB. Psychoactive drugs and human sexual behavior: the role of serotonergic activity. J Psychoactive Drugs 1992; 24:1–40

64. Albertson TE, Walby WF, Derlet RW. Stimulant-induced pulmonary toxicity. Chest 1995; 108:1140–1149

65. Arnett EN, Battle WE, Russo JV, Roberts WC. Intravenous injection of talc-containing drugs intended for oral use. A cause of pulmonary granulomatosis and pulmonary hypertension. Am J Med 1976; 60:711–718

66. Robertson CH Jr, Reynolds RC, Wilson JE III. Pulmonary hypertension and foreign body granulomas in intravenous drug abusers. documentation by cardiac catheterization and lung biopsy. Am J Med 1976; 61:657–664

67. Lewman LV. Fatal pulmonary hypertension from intravenous injection of methylphenidate (Ritalin) tablets. Hum Pathol 1972; 3:67–70

68. Schaiberger PH, Kennedy TC, Miller FC, Gal J, Petty TL. Pulmonary hypertension associated with long-term inhalation of "crank" methamphetamine. Chest 1993; 104:614–616

69. Sperling LS, Horowitz JL. Methamphetamine-induced choreoathetosis and rhabdomyolysis [letter]. Ann Intern Med 1994; 121:986

70. Kendrick WC, Hull AR, Knochel JP. Rhabdomyolysis and shock after intravenous amphetamine administration. Ann Intern Med 1977; 86:381–387

71. Ginsberg MD, Hertzman M, Schmidt-Nowara WW. Amphetamine intoxication with coagulopathy, hyperthermia, and reversible renal failure. a syndrome resembling heatstroke. Ann Intern Med 1970; 73:81–85

72. Screaton GR, Singer M, Cairns HS, Thrasher A, Sarner M, Cohen SL. Hyperpyrexia and rhabdomyolysis after MDMA ("ecstasy") abuse [letter; comment]. Lancet 1992; 339:677–678

73. Callaway CW, Clark RF. Hyperthermia in psychostimulant overdose. Ann Emerg Med 1994; 24:68–76

74. Foley RJ, Kapatkin K, Verani R, Weinman EJ. Amphetamine-induced acute renal failure. South Med J 1984; 77:258–260

75. de Man RA, Wilson JH, Tjen HS. Acute liver failure caused by methylenedioxymethamphetamine ("ecstasy"). Ned Tijdschr Geneeskd 1993; 137:727–729

76. Jones AL, Jarvie DR, McDermid G, Proudfoot AT. Hepatocellular damage following amphetamine intoxication. J Toxicol Clin Toxicol 1994; 32:435–444

77. Johnson TD, Berenson MM. Methamphetamine-induced ischemic colitis. J Clin Gastroenterol 1991; 13:687–689

78. Pecha RE, Prindiville T, Pecha BS, Camp R, Carroll M, Trudeau W. Association of cocaine and methamphetamine use with giant gastroduodenal ulcers. Am J Gastroenterol 1996; 91:2523–2527

79. Cadier MA, Clarke JA. Ecstasy and whizz at a rave resulting in a major burn plus complications. Burns 1993; 19:239–240

80. Deloach-Banta LJ. Lichenoid drug eruption: crystal methamphetamine or adulterants? Cutis 1994; 53:97–98

81. Segar DL. Substances of abuse. Top Emerg Med 1985; 7:18–30

82. Richards JR, Derlet RW, Duncan DR. Methamphetamine toxicity: treatment with a benzodiazepine versus a butyrophenone. Eur J Emerg Med 1997; 4:130–135

83. Gary NE, Saidi P. Methamphetamine intoxication. a speedy new treatment. Am J Med 1978; 64:537–540

Articles

Update on the Status of Africanized Honey Bees in the Western States

KENNETH T. KIM, MD, *Long Beach, California*; JODI OGURO, *Berkeley, California*

The Africanized honey bee (AHB), *Apis mellifera scutella*—perhaps better known as the "killer bee"—has arrived in the western United States and in southern California, following a nearly 50-year northward migration across South and Central America. First detected near Hidalgo, Texas in October 1993, the bees continue to advance 100 to 300 miles per year by colonizing existing hives or forming new hives in the wild. Although the AHB's "killer" reputation has been greatly exaggerated, the presence of AHBs will increase the chances of people being stung.

(Kim KT, Oguro J. Update on the status of Africanized honey bees in the Western states. West J Med 1999; 170:220–222)

As a productive honey bee adapted to the tropical climate, the African honey bee was introduced in Brazil in 1956. By 1957, escaped colonies had become established in the wild, increasing in number dramatically and interbreeding with European honey bees.[1] The result was the Africanized honey bee (AHB).

Comparison of Africanized and European Honey Bees

There are more similarities than dissimilarities between the AHB and the native European honey bee (EHB). Although the AHB is slightly smaller and weighs less (dry weight 14.8 mg vs. 16.6 mg) than the EHB, this difference is undetectable to the common eye.[1] Individual species can only be differentiated by morphometry[2] or mitochondrial DNA.[3] In addition, the individual sting of both types of bees is nearly identical.

About 99% of the time, the behavior of AHBs and EHBs is the same.[1] There is no difference in aggressive or defensive behavior in encounters with individual foraging bees. The difference in the behavior of the two bees occurs only when AHBs perceive that their hives are threatened. They will attack more quickly and in greater numbers than EHBs when disturbed, and will pursue and continually sting a victim over greater distances of up to 0.6 miles.[4] Even slight disturbances such as strange odors or vibrations from a lawn mower can agitate a colony. Another significant difference is that the AHB swarms several times a year, whereas the EHB swarms only once or twice a year. Swarming occurs when new queens are produced in a colony, and part of the colony leaves with the old queen, thereby increasing the number of colonies in an area. The AHBs are relatively indiscriminate in selecting nesting sites, setting up residence in unprotected areas, where they are more easily disturbed. As a result, in areas established with AHBs, there are approximately 12 times more colonies of AHBs than of EHBs. Therefore, the total number of colonies and bees in a geographic area dramatically increases.[1]

Examination of the venom of the two bees also reveals the great similarity between them.[5] The major components of honey bee venom—mellitin, phospholipase A2, and hyaluronidase—appear to be present in similar concentrations in both European and Africanized bee venom.[6] The average content of the venom sac of Africanized bees has been found to be slightly less than that of domestic bees, but the lethality of the venom of Africanized bees in mice is similar to that for domestic bees.[6] The principal risk to victims of Africanized bees lies in the multiplicity of stings sustained.

Many pharmacologically active components are present in bee venom, including peptides, enzymes, and biogenic amines that cause toxic reactions. The most important component is the peptide mellitin, which comprises approximately 50% of bee venom.[1] Mellitin's high toxicity may cause hemolysis, inflammatory reactions, increased capillary permeability, and smooth muscle contraction. Bee venom causing toxic reactions from multiple or massive numbers of bee stings results in universal vulnerability because the reaction is dependent on the amount of venom injected.

From the Allergy, Asthma, and Respiratory Care Center, Inc, Long Beach, California (Dr Kim); and the undergraduate program at the University of California, Berkeley, California (Ms Oguro).

Reprint requests to Kenneth T. Kim, MD, 2501 Cherry Avenue #350, Long Beach, CA 90806.

California

The pace of AHB spread slowed considerably 4 years ago, once these bees reached California's southernmost desert from Arizona, because of adverse conditions.[7] By October 1994, however, they crossed into California, and may owe their newfound headway to favorable feeding conditions spawned by El Nino. The extra rain left the desert carpeted with more vegetation, improving the bees' reproduction rate and providing a kind of bee superhighway to the west and north. By April 1999, AHB colonized territory included all of Imperial, Los Angeles, Orange, San Bernardino, Riverside, and San Diego counties and parts of Ventura and Kern counties.

Currently, though hundreds of swarms and nests have been located, no people have been fatally stung in California. Since the AHB hybrids were first detected, over 20 stinging incidents have been reported in the state. The median number of stings in these attacks is 15 (range 1–500+). Some observers hope that evolutionary forces will make the bees less aggressive by the time they reach heavily populated areas, but this is not likely since they are still very defensive—even after more than 40 years of hybridizing with the less aggressive EHB.

Western States

The first multiple stinging incident in the United States involving the AHB (via natural northward movement) occurred in the spring of 1991 in the lower Rio Grande Valley area of south Texas, with the first massive stinging incident (350 stings) occurring in the fall of 1991. Since the arrival of AHBs in the United States, there have been five deaths associated with attacks by Africanized honey bees—two incidents in Texas and three incidents in Arizona. Even though AHBs do not establish colonies well in freezing climates, much of the continental United States could be threatened to some degree by the AHB during warm seasons due to inadvertent transport of bees by trucks, trains, and other forms of shipping. At the same time, the geographic area from which AHB incidents may arise is growing as the AHB population expands, while the prevalence of the EHB is diminishing as feral honey bee populations become Africanized through hybridization.

Treatment and Management

Evaluation of a stung patient should asses the number of stings and the victim's bee-venom allergic status, body size, and general health. Important historical information includes any insect sting allergy, other complicating medical conditions (eg, cardiovascular or pulmonary disease), and medications, such as beta-blockers. Stingers should be scraped from the patient's neck using a stiff, noncutting instrument (eg, a credit card). There should be no pinching or pulling of stingers, since the remaining venom in the sac could be squeezed into the patient, further intensifying the reaction. While the stingers are being removed, an estimate can be made of the number of stings, to help in the prediction of severity of toxicity.

The anatomic location of stings may increase risk. For example, multiple or massive numbers of stings in the neck area may cause upper airway obstruction. An individual who has a history of large local sting reactions could be at even greater risk. AHBs may have a greater tendency to sting in the head and neck area, and allergic reactions occur more commonly when stings are in this area.

The most common reaction to a hymenoptera sting is local edema, erythema, and pruritus at the sting site, often extending to a major joint. For example, a sting of the hand might cause local swelling extending to the elbow. No further diagnostic treatment is needed for this, and simple analgesics or the application of calamine lotion or cool compresses may help.

There are also systemic reactions to insect stings. The most common systemic reaction is an urticarial reaction, which can progress to anaphylaxis, with bronchoconstriction, laryngeal edema, and hypotension. In the acute setting, if there are clinical signs and symptoms of respiratory compromise or hypotension, epinephrine is the treatment of choice. Diphenhydramine, bronchodilators administered through inhaled and intravenous routes, and oxygen supplement should also be used. Parenteral corticosteroids are also recommended to prevent a late-phase anaphylactic response. If there is swelling in the neck area and upper airway obstruction, the patient may need intubation. Fluid volume expansion often is needed—in addition to supporting circulation, it dilutes the toxic venom components. Vasopressors and mechanical ventilation may be necessary in the most severe cases, while corticosteroids should be considered for control of the inflammatory response. Tetanus vaccination also should be considered.

A child who sustains more than about 10 to 20 bee stings, or an adult who sustains more than about 100 stings, should seek emergency medical attention even in the absence of bee sting allergy, because of the pharmacologic effects of venom constituents. The LD_{50} (lethal dose to kill 50% of the target population) for honey bee venom is estimated to be about 19 stings per kg of body weight. Bee venom contains several complex toxins which, in high doses, can even affect individuals who do not have bee allergy.

Individuals manifesting symptoms of systemic anaphylaxis have a 35% to 60% risk of recurrent anaphylaxis, and therefore should be considered for desensitization treatment, also known as venom immunotherapy. This can protect individuals with well documented hymenoptera sensitivity. Venom immunotherapy, using escalated doses of venom as allergen, prevents recurrent systemic reactions to bee stings in 95% to 99% of patients.[8] Although dosing intervals and a final maintenance dose and schedule are often individually determined, a typical maintenance program is 100 micrograms of venom given every 4 to 6 weeks. Indications for venom immunotherapy are a

history of systemic reaction to bee stings (except for urticaria only), and evidence of IgE to the relevant venom as demonstrated by skin testing or radioallergosorbent test (RAST) testing. Hypersensitive individuals who spend a substantial amount of time outdoors, whether for employment or recreation, should be considered for desensitization. Otherwise, hypersensitive persons who decline treatment should minimize their risk of exposure to bee stings, and be proficient with self-administration of epinephrine.

Africanized honey bee attacks are associated with multiple stings that can lead to toxic reactions from the sheer dosage of venom delivered.[9] Clinical manifestations include rhabdomyolysis, myoglobinuria, acute renal failure,[10] myocardial infarction, and acute hemorrhagic pancreatitis.[11] At least one of the five deaths was secondary to delayed renal failure, thus underscoring the importance of careful followup monitoring after the initial anaphylactic reaction has been treated. Since no antivenom is available, treatment is largely supportive.

Practical Advice

Africanized honey bees are much less selective in choosing nesting sites than EHBs. The typical EHB hive is in a tree or in a hole of a tree, while AHBs frequently select holes in walls or in the ground, under mobile homes, in old tires, and so on. Unfortunately, these unexpected nesting sites lead to more unexpected encounters. Beekeepers and certain gardeners may need to change some of their practices, since the operation of machinery (tractors, lawn mowers, and weed eaters) in the general area of an AHB hive is the most common source of unintentional disturbance.

If one disturbs a nest or hive of bees, the best advice is to run away as quickly as possible, covering the head with a collar or shirt without obscuring vision. Lying down, huddling under clothing or some other partial protection, or submerging oneself in water will not help. The EHB may pursue a victim for up to five hundred yards, whereas the AHB has been known to follow its victim for as far as half a mile—most people can outrun a swarm of these bees. Swatting at the bees while running is also not helpful—instead, a pursued person should concentrate on retreating indoors or into a car if possible. Once the victim is in a safe place, he or she can be covered with a blanket, rinsed off with water to remove any remaining bees, and taken to an emergency room.

Children are potentially at increased risk for being victims of massive attacks by AHBs due both to their decreased ability to recognize potential stinging situations and to the toxicity of large amounts of venom relative to their smaller bodies. Elderly individuals and those with severe diseases are also at increased risk because of their bodies' relative intolerance to large toxic exposures. Another common risk factor of the elderly is their inability to quickly escape a dangerous situation. Certainly, individuals of any age with significant cardiovascular and pulmonary diseases are at an increased risk.

Common sense preventive measures have been outlined in a recent public health bulletin:[12]

1) Avoid direct contact with and excessive motion or noise around bee colonies. Never attempt to move or destroy feral beehives, but report their location to the authorities.

2) When outdoors near bee colonies, wear shoes, long pants, and long sleeves. Avoid wearing perfumes or dark colored clothing and keep pets on a leash.

3) Eliminate sites for possible colonization including any holes and defects in exterior walls greater than ⅛ inch and junk piles in yards. Inspect premises routinely to identify any new colonies.

4) Persons with potential occupational exposure to AHBs (eg, first emergency responders, landscapers, and park rangers) should have special training on this topic.

Because there are characteristically more AHBs per given area than EHBs, and because of their more aggressive defensive behavior, both the bee-venom sensitive individual and the general population are at increased risk of coming in contact with these bees in areas where they reside. The effect of multiple stings that may occur with these bees is likely to lead to greater toxicity.

In 1993, the Los Angeles County Africanized Honey Bee Task Force was formed. The task force includes the fire vector districts, the county sheriff's department, the superintendent of schools, the US Forest Service, and other agencies and individuals. A special toll-free number, 800-925-3800, is available for bee-related matters. As the AHB migrates and colonizes the West, there will inevitably be more AHB–human encounters, but their overall impact may be minimized by common sense preventive measures and prompt emergency response and medical services.

REFERENCES

1. McKenna W. Killer bees: what the allergist should know. Pediatr Asthma Allergy and Immunol 1993; 6:275–285

2. Sylvester HA, Rinderer TE. Fast Africanized bee identification system (FABIS) manual. Am Bee J 1987; 127:511–516

3. Crozier YC, Koullanos S, Crozier RH. An improved test for Africanized honeybee mitochondrial DNA. Experientia 1991; 47:968–969

4. Winston ML. Killer Bees, the Africanized Honeybee in the Americas. Cambridge, MA, Harvard University Press, 1992

5. Schumacher MJ, Schmidt JO, Egen NB, Lowry JE. Quantity, analysis and lethality of European and Africanized honeybee venoms. Am Trop Med Hyg 1992; 43:79–86

6. Schumacher MJ. Significance of Africanized bees for public health. Arch Med Intern 1993; 155:2038–2043

7. Kim KT. Insect stings [letter]. N Engl J Med 1994; 331:1776

8. Hunt KJ, Valentine MD, Sobotka AK, Benton AW, Amodio FJ, Lichtenstein LM. A controlled trial of immunotherapy in insect hypersensitivity. N Engl J Med 1978; 299:157–161

9. Franca FOS, Benvenuti LA, Fan HW, et al. Severe and fatal mass attacks by "killer" bees (Africanized honeybees—*Apis mellifera scutellata*) in Brazil; clinicopathological studies with measurement of serum venom concentrations. Q J Med 1994; 87:269–282

10. Hommel D, Bollandard F, Hulin A. Multiple African honeybee stings and acute renal failure. Nephrology 1998; 78:235–236

11. Daisley H. Acute haemorrhagic pancreatitis following multiple stings by Africanized bees in Trinidad. Royal Soc Trop Med Hyg 1998; 92:71–72

12. California Department of Health Services. Africanized honeybees in California: public health aspects. California Morb 1998

Mass Envenomations by Honey Bees and Wasps

RICHARD S. VETTER, MS; P. KIRK VISSCHER, PHD; *Riverside, California;*
SCOTT CAMAZINE, MD, PHD, *University Park, Pennsylvania*

Stinging events involving honey bees and wasps are rare; most deaths or clinically important incidents involve very few stings (<10) and anaphylactic shock. However, mass stinging events can prove life-threatening via the toxic action of the venom when injected in large amounts. With the advent of the Africanized honey bee in the southwestern United States and its potential for further spread, mass envenomation incidents will increase. Here we review the literature on mass stinging events involving honey bees and wasps (ie, yellowjackets, wasps, and hornets). Despite different venom composition in the two insect groups, both may cause systemic damage and involve hemolysis, rhabdomyolysis, and acute renal failure. Victim death may occur due to renal failure or cardiac complications. With supportive care, however, most victims should be able to survive attacks from hundreds of wasps or approximately 1000 honey bees.

(Vetter RS, Visscher PK, Camazine S. Mass envenomations by honey bees and wasps. West J Med 1999; 170:223–227)

Death from honey bee or wasp envenomation is a rare event. Most often it is caused by IgE-mediated Type I anaphylaxis, and the fatal incident involves a single sting. Fatal stings usually occur in the head or neck; death typically occurs from hypotension, laryngeal edema, or bronchial constriction within 1 hour, and the typical victim is over 40 years of age, with arteriosclerosis playing a contributing role.[1] Less commonly, death occurs from the toxic effects of massive envenomation involving hundreds to thousands of stings. Here we review incidents of massive envenomations and discuss the differences between bees and wasps, their venoms, and potential for danger. With the recent arrival of the Africanized honey bee in the United States (the states bordering Mexico[2] and, recently, Nevada) as well as the potential for their spread in the southeastern United States, there is concern that the incidence of stinging deaths will increase.

Bee vs. Wasp

Both bees and wasps inflict painful stings, but it is useful to distinguish one from the other. In the medical literature one repeatedly encounters confusion over the insect responsible for stinging. We clarify the distinction, which may be important for proper treatment.

Most bees and wasps (both of the insect order Hymenoptera) live solitary lives and are not predisposed to sting humans. The greatest threat to humans is posed by a few species of social bees—mainly honey and bumble bees (Family Apidae); and social wasps—hornets, yellowjackets, and paper wasps (Family Vespidae); which produce large colonies of sterile workers. Nests of paper wasps (*Polistes*) and bumble bees typically contain only 100–200 insects and are not often involved in mass stinging events, so they are not discussed in this review.

The typical hymenopteran stinging event occurs when a single insect, usually a yellowjacket wasp, is disturbed while searching for food. This usually occurs in the late summer and early fall, when large numbers of hungry yellowjackets are attracted to the food of humans eating outdoors.[3] Any wasp or bee will sting in defense if it is accidentally stepped on, swatted, or otherwise disturbed.

In contrast, mass envenomations occur when stinging insects respond to a human intruder as a threat to their colony. Typically, this happens when someone inadvertently stumbles into a colony or otherwise disturbs the structure in which they live (eg, by throwing rocks at, shooting at, or chopping a tree containing the colony), whereupon hundreds or thousands of stinging insects may issue forth in defense.

Originally a European and African species, the honey bee, *Apis mellifera*, is used throughout the world by beekeepers; therefore, it is the bee species most commonly involved in stinging incidents. Additional envenomations have been recorded from other honey bee (*Apis*) species in Asia, including the Asian honey bee (*A cerana*) and the giant honey bee (*A dorsata*). All honey bee species live in colonies of several thousand workers. Managed honey bee colonies consist of about 40,000 workers, with Africanized honey bees having slightly smaller colonies.

From the Department of Entomology, University of California, Riverside, Riverside, California (Mr Vetter and Dr Visscher); and the Department of Entomology, Penn State University, University Park, Pennsylvania (Dr Camazine).

Reprint requests to Rick Vetter, Department of Entomology, University of California Riverside, Riverside, CA 92521 (e-mail: vetter@citrus.ucr.edu).

Yellowjackets (*Vespula* and *Dolichovespula*, 10–15 mm in length) and hornets (*Vespa*, 15–40 mm) maintain colonies of several hundred to a few thousand individuals.[4] In comparison to yellowjackets, which maintain comparatively larger colonies, *Vespa* hornets are more dangerous because of their greater venom injection capability and greater venom toxicity. *Vespa* wasps are distributed mostly in Europe and Asia,[4] with one species (*Vespa crabro*) established in the northeastern United States.[5] Yellowjackets are originally holarctic in distribution, but have become established in tropical and subtropical regions such as Australia, New Zealand, Hawaii, South America, and South Africa, where they have become serious economic pests.[6]

Sting versus Bite

A sting is delivered by a posterior, tapered, needle-like structure designed to inject venom. In contrast, a bite is delivered with mouthparts. Scorpions, ants, bees, and wasps have stings. The stings of bees and wasps are painful and potentially dangerous, whereas their bites cause minor irritation. Ants may cause damage with both a venomous sting and a noxious bite.[7] Spiders and centipedes have venomous bites that inject venom through specialized oral structures such as fangs.

Honey bee stings have an unusual specialization: their stings are strongly barbed and are designed to remain imbedded in mammalian flesh, whereas wasp stings are not. This presence or absence of a detached sting can aid in determining whether envenomation is caused by bees or wasps. This can be critical in allergic individuals, since the venom allergens differ between the two insect groups. However, in mass envenomations involving a nonallergic victim, there is less of a need to make this distinction; although the venom dose lethal to 50% of victims (LD_{50}) differs amongst the insects, clinical care can be guided by symptomatic treatment based upon the degree of systemic toxicity.

Venom

As reviewed by Banks and Shipolini,[8] honey bee venom is similar among the different *Apis* species, with minor variations in component quantities. Melittin (50% by dry weight) is the main pain-inducing compound, which functions by altering membrane integrity. The larger molecular-weight enzyme, phospholipase A_2 (11%), works in concert with melittin; it has no cytolytic effect by itself.[9,10] These two components are responsible for red-cell hemolysis. Once melittin has disrupted the membrane, phospholipase A_2 cleaves bonds in the fatty acid portion of the bilipid membrane layer; it also is the major allergen in bee venom. Mast-cell degranulating protein (2%), as its name implies, causes mast cells to break down, releasing histamine. Hyaluronidase (1%–2%) is a secondary allergen; it also disrupts the hyaluronic acid connective-tissue matrix, making it a "spreading factor" that allows the other venom components to infiltrate tissues. Hyaluronidase is a component found in the venoms of a variety of evolutionarily diverse animals (eg, snakes and spiders).[11] Additional enzymes include acid phosphatase (1%) and lysophospholipase (1%). Bee venom also contains a neurotoxic peptide, apamin (3%). Histamine is only a minor portion of bee venom (0.7%–1.6%); histamine reaction from honey bee envenomation is due to endogenous release initiated in the victim by other venom factors.

Because of the greater taxonomic diversity of wasps, wasp venoms are more variable in their composition among species. In general, they contain active amines (serotonin, histamine, tyramine, catecholamines); wasp kinins (similar in composition to bradykinins), which are mostly responsible for pain; and histamine-releasing peptides (mastoparans), which are responsible for the inflammatory response. Of the allergens, "Antigen 5" is the most active. Of the lesser active allergens, phospholipase A and B cleave the fatty acids of the bilipid layer at the 1 position, and hyaluronidase is a spreading factor.[12,13] Some wasp venoms have neurotoxins (eg, mandaratoxin in *Vespa mandarinia*), and the venom of a few species contains acetylcholine.[12]

Mass Stinging Incidents

Most of the mass envenomation cases reported in the medical and entomological literature involve hundreds of stings, many resulting in toxic systemic reactions and renal failure.[14–55] Often, the sting totals reported in the literature are estimates or are counts of the *minimum* number of stings removed from the victim. Some case histories were excluded from this study because sting totals were listed ambiguously (eg, "numerous", or "dozens") although one case history[23] reported as "mulitple" involved 150–250 stings (B. Ariue, MD, Department of Pediatrics, Kaiser Permanente, Lancaster, CA, written communication, 1997). We also omitted a few mass stinging incidents in which death occurred within 1–2 hours, because death in these cases was probably due to anaphylaxis rather than venom toxicity.

Massive wasp attacks range from tens to hundreds of stings whereas honey bee attacks can reach several thousand stings, reflecting differences in colony size (Fig. 1). Stings in the head and neck predominate because these insects preferentially attack these areas. Renal failure or death may occur in the range of 20–200 wasp stings and 150–1000+ honey bee stings (Fig. 1). In cases where it was not reported whether acute renal failure (ARF) developed, death may have quickly occurred before systemic damage was evident. The human LD_{50} for honey bee stings has been estimated to be between 500–1200 stings.[56,57] With medical treatment, many victims with 1000+ honey bee stings have survived.[14–22]

Only a weak relationship exists between age and the outcome of mass sting attacks (Fig. 2). Both older and very young victims appear to succumb more easily to bee stings but not wasp stings—but the scant and variable data cannot resolve this. Surprisingly, despite children's small body mass, several stinging incidents of 200–1000+ honey bee stings with subsequent hospitalization resulted in recovery.[22–24]

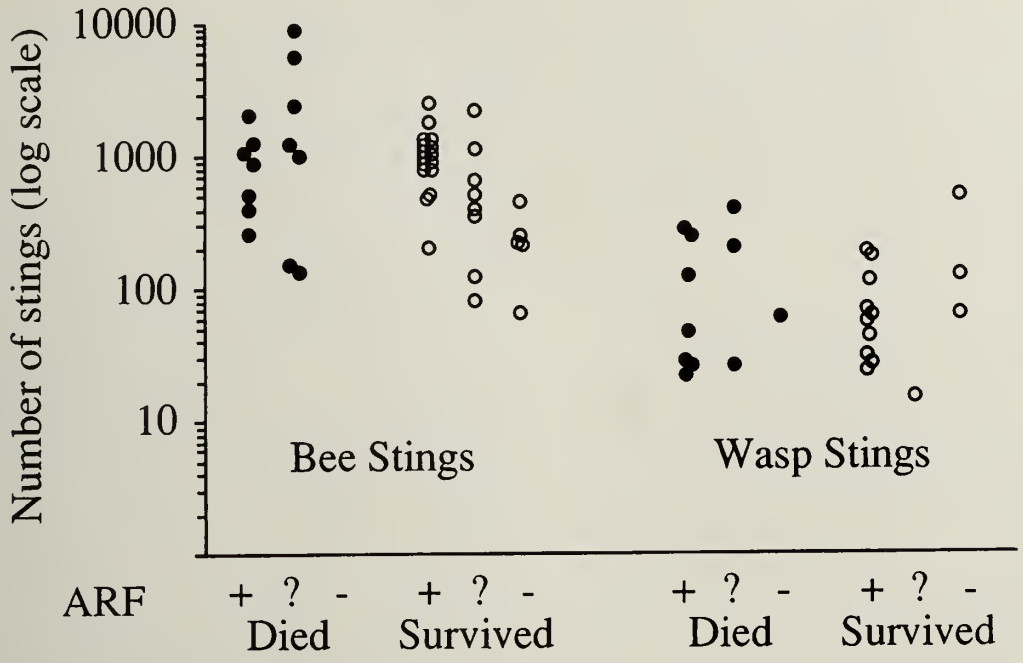


Figure 1.—The number of bee or wasp stings is plotted against the outcome of the stinging incident (died ●, survived ○). Under categories of "died" or "survived", the data are separated into categories of whether acute renal failure (ARF) was observed (+), did not occur (–), or was not evident from the case history (?). Sting estimates were scored as 110% of the reported numerical value for ease of graphing (eg, "1000+" is displayed as "1100" on the graph); in cases of multiple overlapping values, the data points are clustered around the value as best possible).

Children still are at high risk because they are more likely to be stung due to carelessness, and are less able to escape when stung.

Clinical stinging attacks from wasps involve fewer insects, but there were more deleterious effects from their stings than from a similar number of honey bee stings (Fig. 1). Deaths from massive wasp attack[25–32] are most often the result of attacks by *Vespa orientalis* and *Vespa affinis*. These large eastern hemisphere wasps have killed, via acute venom toxicity, with less than 300 stings. Mammalian toxicity tests on mice show that honey bee venom LD_{50} (3 mg/kg) is about equivalent to that of the larger hornets (*Vespa* spp), and yellowjacket wasp (*Vespula* [=*Paravespula*] spp) venom is about 3-fold less toxic.[57]

Pharmacological Effects of the Venom

In individuals who are not allergic to venom, small numbers of stings cause little systemic damage, and the response is limited to a localized wheal at the sting site, with edema, erythema, and pruritis. Symptomatic treatment is all that is required.

Despite differences between bee and wasp venoms, their pharmacological effects are somewhat similar. In massive envenomations, initial symptoms include edema, fatigue, dizziness, nausea, vomiting, fever, and unconsciousness. Endogenous histamine response can cause quick onset of diarrhea and incontinence;[19,33,34] in one case the victim defecated bees he had swallowed while still under attack.[19] Systemic damage may develop within 24 hours, although there are instances of delayed onset (2–6 days).[35,36] Systemic effects include hemolysis with its associated hematoglobinuria and hematoglobinemia. Rhabdomyolysis may occur, leading to serum elevations of creatinine phosphatase (CPK) and lactate dehydrogenase; CPK levels of 91,000 IU/liter have been reached within 24 hours of mass stinging by bees (normal <160 IU/liter).[16] The venom does not appear to affect the smooth or cardiac muscle.[32] Hepatic serum enzyme levels may be elevated. Thrombocytopenia can occur without evidence of disseminated intravascular coagulation.[36] Oliguria and ARF due to acute tubular necrosis are common (Fig 1). Damage is usually reversible, responding well to dialysis; complete recovery may require 3–6 weeks. Although typically indirect renal damage is thought to result from the breakdown of blood cells or muscle tissues, there may be a direct nephrotoxic effect since ARF can occur without rhabdomyolysis or hemolysis.[14,37] Other symptoms include muscular aches, cramps, hyperkalemia, hyperglycemia, and hypertension. In contrast, a pediatric case of 120 German yellowjacket (*Vespula germanica*) stings in a 3 1/2-year-old child showed no serum abnormalities but instead showed central nervous system aberrations (eg, hallucinations).[38]

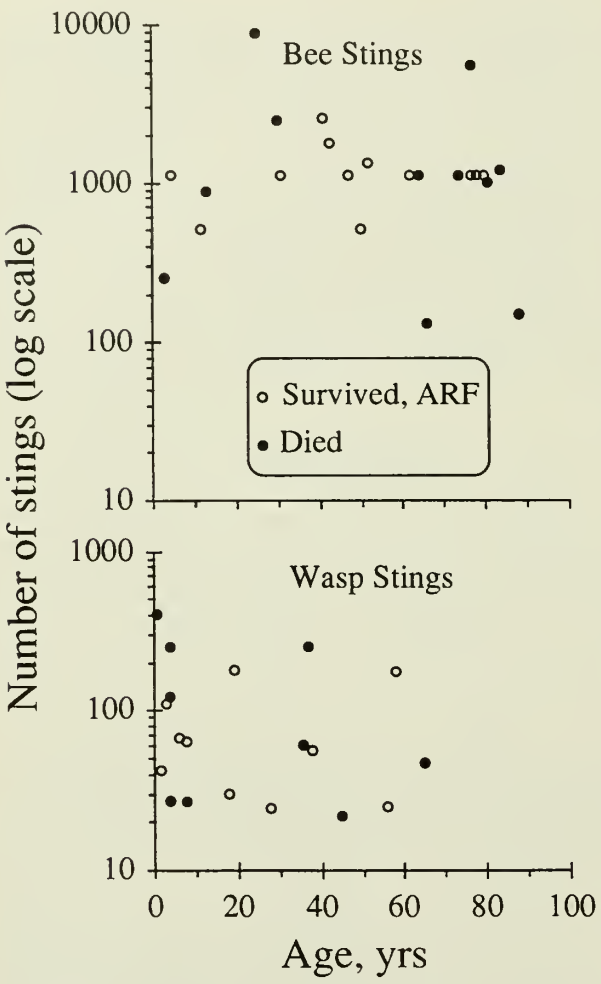


Figure 2.—The number of bee and wasp stings is plotted against age showing envenomations resulting in death (●) or survival with renal damage (○). Case reports from Figure 1 where renal failure did not occur or could not be definitively determined from the report were not included here. Sting estimates were scored as 110% of the reported numerical value for ease of graphing (eg,"1000+" is displayed as "1100" on the graph); in cases of multiple overlapping values the data points are clustered around the value as best possible.

Death has occurred within 16 hours to 12 days after the stinging incident for honey bee stings,[18,21,39–44] (An 88-year-old female died 4 days after receiving 100–200 Arizona Africanized honey bee stings; a 66-year-old convalescing male died 12 days after receiving about 130 stings [J. O. Schmidt, PhD, US Department of Agriculture, written communication, 8 October 1997]). Death has occurred within 4 hours to 9 days for wasp stings.[25–32,45] Fatalities are typically the result of renal failure due to breakdown products of hemolysis, myolysis, and the ensuing renal damage; or from cardiac arrest due to complications of the venom toxicity. Fatal cases include victims who were sent home after initial examination, only to return the next day with graver symptoms.[25,28]

Emergency Assessment and Treatment of a Mass-Envenomated Victim

Mass envenomations only occur near colonies of stinging insects. If attacked by large numbers of stinging insects, a person's best defense is to run away from the colony as quickly as possible, as the insects will not continue pursuit outside their territorial range. Honey bees will leave detached stings in the victim, and these should be removed as soon as possible by whatever method is quickest. Erroneous conventional medical advice states that the venom sac should never be squeezed, since this purportedly injects more venom into the victim; however, this was recently shown to be incorrect.[58] Removal of bee stings that have been embedded for more than one minute will have little or no effect in reducing envenomation since most of the venom empties from detached honey bee stings within 10–20 seconds.[59] Emergency personnel should be alert to living bees or wasps still entangled in the victim's clothing,[38,46] since this could create additional problems by exposing hypersensitive attending medical personnel to stings.

Blood chemistry studies performed over a period of hours to days will reveal whether toxic venom effects have occurred. Particular attention should be paid to serum levels of hemoglobin and myoglobin. Patients should be admitted for observation, as delayed onset of serious symptoms may occur. If a victim is involved in a mass stinging incident of several hundred wasp stings or 1000+ honey bee stings, careful observation in a hospital setting and supportive care will often be sufficient to overcome the toxic effects of the venom, and most patients can be expected to recover.

Acknowledgments

We thank the following individuals for translation help: L. Merrill, H. Hutchinson, and S. Triapitsyn.

REFERENCES

1. Meier J. Biology and distribution of hymenopterans of medical importance, their venom apparatus and venom composition. In Meier J, White J (Eds). Handbook of Clinical Toxicology of Animal Venoms and Poisons. Boca Raton, FL, CRC Press, 1995, pp 331–348

2. Visscher PK, Vetter RS, Baptista FC. Africanized bees, 1990–1995: initial rapid invasion has slowed in the US Calif Agric 1997; 52:22–25

3. Edwards R. Social Wasps; Their Biology and Control. East Grinstead, UK, Rentokil Ltd, 1980

4. Spradbery JP. Wasps. Seattle, WA, University Washington Press, 1973

5. Akre RD, Greene A, MacDonald JF, Landolt PJ, Davis HG. The Yellowjackets of America North of Mexico. USDA handbook #552, 1980

6. Edwards R. The world distribution pattern of the German wasp, *Paravespula germanica* (Hymenoptera: Vespidae). Entomol Germ 1976; 3:269–271

7. Vetter RS, Visscher PK. Bites and stings of medically important venomous arthropods. Int J Dermatol 1998; 37:481–496

8. Banks BEC, Shipolini RA. Chemistry and pharmacology of honey-bee venom. In Piek T (Ed). Venoms of the Hymenoptera: Biochemical, Pharmacological and Behavioural Aspects. Orlando, FL, Academic Press, 1986, pp 329–416

9. Vogt W, Patzer P, Lege L, Oldigs H-D, Wille G. Synergism between phospholipase A and various peptides and SH-reagents in causing haemolysis. Naunyn-Schmeid Arch Pharmak 1970; 265:442–454

10. Mollay C, Kreil G. Enhancement of bee venom phospholipase A2 activity by melittin, direct lytic factor from cobra venom and polymyxin B. FEBS Lett 1974; 46:141–144

11. Meier J, White J, (Eds). Handbook of Clinical Toxicology of Animal Venoms and Poisons. Boca Raton, FL, CRC Press, 1995

12. Nakajima T. Pharmacological biochemistry of vespid venoms. In Piek T, (Ed). Venoms of the Hymenoptera: Biochemical, Pharmacological and Behavioural Aspects. Orlando, FL, Academic Press, 1986, pp 309–327

13. Hoffman DR. Hymenopteran venom proteins. Adv Exp Med Biol 1996; 391:169–186

14. Beccari M, Castiglione A, Cavaliere G, d'Aloya G, Fabbri C, Losi B, et al. Unusual case of anuria due to African bee stings. Int J Artif Organs 1992; 15:281–283

15. Hiran S, Pande TK, Pani S,Gupta R, Vishwanathan KA. Rhabdomyolysis due to multiple honey bee stings. Postgrad Med J 1994; 70:937

16. Humblet Y, Sonnet J, van Ypersele de Strihou C. Bee stings and acute tubular necrosis. Nephron 1982; 187–188

17. McKenna WR. Characteristics of multiple–massive honey bee sting cases. J Allergy Clin Immunol 1994; 93:224

18. Mejia G, Arbelaez M, Henao JE, Sus AA, Arango JL. Acute renal failure due to multiple stings by Africanized bees. Ann Intern Med 1986; 104:210–211

19. Murray JA. A case of multiple bee stings. Cent Afr J Med 1964; 10:249–251

20. Patrick A, Roberts L, Poon-King P, Jeelal V. Acute renal failure due to multiple stings by Africanized bees report of the first case in Trinidad. West Indian Med J 1987; 36:43–44

21. Rosenfeld G. Human envenomation by bee stings. In Rosenberg P (Ed). Toxins: Animal, Plant and Microbial. Oxford, UK, Pergamon Press, 1976, pp 692–693

22. Tumwine JK, Nkrumah FK. Acute renal failure and dermal necrosis due to bee stings: report of a case in a child. Cent Afr J Med 1990; 36:202–204

23. Ariue B. Multiple Africanized bee stings in a child. Pediatrics 1994; 1:115–117

24. Kini PG, Baliga M, Bhaskaranand N. Severe derangement of the coagulation profile following multiple bee stings in a 2-year-old boy. Ann Trop Paediatr 1994; 14:153–155

25. Barss P. Renal failure and death after multiple stings in Papua New Guinea. Med J Austr 1989; 151:659–663

26. Day JM. Death due to cerebral infarction after wasp stings. Arch Neurol 1962; 7:184–186

27. Gädeke R, Helwig H, Otto M, Schindera F, Weineck B. Tödliche vergiftungskrankheit eines Kindes nach massenhaften Wespenstichen. Med Klin 1977; 1487–1492

28. Hoh TK, Soong CL, Cheng CT. Fatal haemolysis from wasp and hornet sting. Singapore Med J 1966; 7:122–126

29. Korman SH, Jabbour S, Harari MD. Multiple hornet (*Vespa orientalis*) stings with fatal outcome in a child. J Paediatr Child Health 1990; 26:283– 285

30. Sakhuja V, Bhalia A, Pereira BJG, Kapoor MM, Bhusnurmath SR, Chugh KS. Acute renal failure following multiple hornet stings. Nephron 1988; 49:319–321

31. Scragg RFR, Szent-Ivany JJH. Fatalities caused by multiple hornet stings in the territory of Papua and New Guinea. J Med Entomol 1965; 2:309–313

32. Shilkin KB, Chen BTM, Khoo OT. Rhabdomyolysis caused by hornet venom. Br Med J 1972; 1:156–157

33. Jex-Blake AJ. Bee stings. East Afr Med J 1942; 19:74–86

34. Koszalka MF. Multiple bee stings with hemoglobinuria and recovery: report of a case. Bull US Army Med Dept 1949; 9:213–217

35. Borochowitz Z, Hardoff D. Severe late clinical manifestations after hornet (*Vespa orientalis*) stings—in a young child. Eur J Pediatr 1982; 139:91–92

36. Bousquet J, Huchard G, Michel FB. Toxic reactions induced by hymenoptera venom. Ann Allergy 1984; 52:371–374

37. Nace L, Bauer P, Lelarge P, Bollaert PE, Larcan A, Lambert H. Multiple European wasp stings and acute renal failure. Nephron 1992; 61:477

38. Levick N, Braitberg G. Massive European wasp envenomation of a child. Emerg Med 1996; 8:239–245

39. Franca FOS, Benvenuti LA, Fan HW, Dos Santos DR, Hain SH, Picchi-Martins FR, et al. Severe and fatal mass attacks by "killer bees" (Africanized honey bees—*Apis mellifera scutellata*) in Brazil: clinicopathological studies with measurement of serum venom concentrations. Quart J Med 1994; 87:269–282

40. Gillmore JH. A case of circulating plasma antithromboplastin as a result of bee stings. East Afr Med J 1963; 40:639–642

41. Irvine ROH. The twin-coil artificial kidney in the treatment of acute oliguric renal failure. N Z Med J 1962; Apr:184–190

42. Moret C, Enzel C, Leclercq M, Bosson L, Lecompte J. Un cas d'envenimation mortelle par piqures miltiples d'abeilles (*Apis mellifera* L.). Rev Méd Liège 1983; 38:815–22

43. Ring J, Gottsmann M, Drzybilla B, Eisenmanger W. Tod nach 1000 Bienenstichen. München Med Wochenschr 1986; 128:339–342

44. Schmidt JO. Allergy to venomous insects. In Graham J, (Ed). The Hive and the Honey Bee. Hamilton, IL, Dadant & Sons, 1992, pp 1209–1269

45. Wey W. Wespenstichverletzungen mit tödlichem Ausgang. Schweiz Med Wochenschr 1956; 86:339–340

46. James ES, Walker WG. ACTH in the treatment of multiple wasp stings. CMAJ 1952; 67:50–51

47. Beck BF. Bee Venom Therapy: Bee Venom, Its Nature, and Its Effect on Arthritic and Rheumatoid Conditions. New York, NY, D Appleton-Century Co, 1935

48. Beven JO. "Acidosis" following bee-stings. Lancet 1920; 2:850

49. Boreham MM, Roubik DW. Population change and control of Africanized honey bees (Hymenoptera: Apidae) in the Panama Canal Area. Bull Entomol Soc Am 1987; 33:34–37

50. Ghosh K, Singh S, Pereira BJG, Singhi SC. Acute systemic toxic reactions caused by hornet stings. Indian Pediatr 1988; 25:796–798

51. Kononenko NM, Fesenko IP. Acute kidney damage caused by bee venom after multiple stings [in Russian]. Vrachebure Delo 1974; 1:116–117

52. Lim P, Tan IK, Feng PH. Elevation serum enzymes in patients with wasp/bee sting and their clinical significance. Clin Chim Acta 1976; 66:405–409

53. Muñoz-Arizpe R, Valencia-Espinoza L, Veláquez-Jones L, Abarca-Franco C, Gamboa-Marrufo J, Valencia-Mayoral P. Africanized bee stings and pathogenesis of acute renal failure. Nephron 1992; 61:478

54. Rowe SF, Greer KE, Hodge RH Jr. Electrocardiographic changes associated with multiple yellow jacket stings. South Med J 1979; 72:483–485

55. Weizman Z, Mussafi H, Ishay JS, Shvil Y, Goitein K, Livni N, et al. Multiple hornet stings with features of Reye's syndrome. Gastroenterology 1985; 1407–1410

56. Michener CD. The Brazilian bee problem. Annu Rev Entomol 1975; 20:399–416

57. Schmidt JO. Hymenopteran venoms: striving toward the ultimate defense against vertebrates. In Evans DL, Schmidt JO (Eds). Insect Defenses: Adaptive Mechanisms and Strategies of Prey and Predators. Albany, NY, State University New York Press, 1990, pp 387–419

58. Visscher PK, Vetter RS, Camazine S. Removing bee stings. Lancet 1996; 348:301–302

59. Schumacher MJ, Tveten MS, Egen NB. Rate and quantity of delivery of venom from honeybee stings. J Allergy Clin Immunol 1994; 93:831–835

Articles

Description of an Ethics Curriculum for a Medicine Residency Program

HENRY J. SILVERMAN, MD, MA, *Baltimore, Maryland*

This paper examines the attempts to develop and implement an ethics curriculum for the Internal Medicine Residency Program at the University of Maryland Medical Center. The objectives of the curriculum were to enhance moral reasoning skills and to promote humanistic attitudes and behavior among the residents. The diverse methodologies used to achieve these objectives included case discussions, literature reading, role playing, writing, and videos. These activities occurred predominantly within the forum of morning report sessions and ethics ward rounds. The author also describes efforts to overcome the initial constraints associated with the implementation of this curriculum and concludes by exploring future directions for the curriculum.

(Silverman HJ. Description of an ethics curriculum for a medicine residency program. West J Med 1999; 170:228–231)

The incorporation of medical ethics into the education of physicians has gained widespread acceptance during the last decade. By 1994, medical ethics was part of the required curriculum in every medical school in the United States.[1] Furthermore, the American Board of Internal Medicine makes the teaching of medical ethics a requirement in its published residency curriculum guidelines, and its Internal Medicine Residency Review Committee stresses the importance of medical ethics in the training of compassionate, effective, humane physicians.[2] Teaching medical ethics in postgraduate programs is important for several reasons. First, patient encounters during the residency years provide opportunities to demonstrate the practical contributions of ethics to medical practice.[3] Second, as residency training occurs at a time when individuals are still constructing their attitudes, beliefs, and behaviors, efforts in ethics education may have a profound and lasting impact on residents. Finally, expanding clinical responsibilities during residency training provide residents with numerous opportunities with which to operationalize their knowledge of medicine and attitudes regarding the practice of medicine. Subsequently, these experiences contribute greatly to residents' ultimate practice styles.

The teaching of medical ethics in residency programs may, however, be problematic due to contingencies of structure and constraints on time, funds, and faculty availability. For example, the structure of a residency program may preclude the teaching of a coherent syllabus that builds upon previous presentations, as residents may find it difficult to attend successive sessions. Additionally, the existence of an overcommitted 3-year training period that struggles to accommodate the essential elements in the broad specialty of internal medicine may prevent an appropriate allotment of time to the teaching of medical ethics. The busy time schedules of the housestaff physicians may also preclude meaningful reflection on and exploration of many complex or emotionally charged subjects. Finally, faculty availability may be an issue due to either the lack of funds or the unavailability of individuals with the proper expertise to teach medical ethics (eg, physicians with formal training in ethics or philosophers with clinical exposure).

Another important issue involves adopting goals for an ethics curriculum, which in turn will determine course content and pedagogical methods. For example, curricula embracing goals centered on enhancing knowledge and moral reasoning skills will consist predominately of large-group presentations and small-group case discussions on traditional topics (eg, ethical theories, moral principles, codes of medical ethics, confidentiality, and euthanasia). Alternatively, curricula may move beyond this traditional model with the aim of promoting humanistic qualities and behavior. Such curricula have incorporated literature, art, film, and writing to stimulate discussions and enhance reflection, as well as the use of role-playing sessions to strengthen interactional skills.[3–5] Recently, commentators have explored the different

From the Department of Medicine, University of Maryland School of Medicine, Baltimore, Maryland.

Reprint requests to Henry J. Silverman, Professor of Medicine, University of Maryland School of Medicine, 10 South Pine Street, Baltimore, MD 21201 (e-mail:hsilverm@umaryland.edu).

goals and methodology being embraced by medical ethics curricula.[1,6] To add to the continuing discussion on teaching medical ethics in postgraduate education, I describe herein the ongoing process of instituting an ethics curriculum in the Internal Medicine Residency Program at the University of Maryland Medical Center.

Description of Curriculum

Curriculum Goals

The enhancement of moral reasoning skills as well as the promotion of humanistic attitudes and behavior were the broad objectives that motivated the development of a medical ethics curriculum for the residency teaching program. The specific goals were:

1) Introduce to residents *basic concepts* in ethics, such as autonomy, determination of competence, the ethics of surrogate decision making, forgoing of life-sustaining treatments, and futility.

2) Enhance the ability of residents to *recognize and appreciate* the ethical dimensions of clinical practice.

3) Increase the ability of residents to *analyze and formulate* well-reasoned positions (ie, to place more emphasis on the process of moral deliberation rather than its conclusions).

4) Promote the *interaction skills* necessary for carrying out ethically sound medicine.

5) Enhance humanism among the residents by conveying to residents the *attitudes, values, and behaviors* needed to deliver care in a compassionate and caring manner.

Faculty

Funding (10% salary support) was made available to the author, an internal medicine faculty member with an MA in bioethics, to develop an ethics curriculum in the Internal Medicine Residency Program.

Curriculum Structure

Several constraints of the residency program were considered in developing the ethics curriculum. First, the structure of the residency program precluded the availability of block time to offer a core curriculum to which every resident in the training program would be exposed. Second, a separate time period was not available to introduce yet another lecture or conference into the residents' busy schedule. To overcome these constraints, the Internal Medicine Residency Program director and the chief residents sanctioned the availability of a monthly morning report conference to the ethics curriculum. Implementation of monthly ethics ward rounds on each of the medical wards was also approved. Finally, a 2- or 4-week ethics elective was made available to the residents. Within the structure of morning report, ethics rounds, and the ethics elective, different pedagogical methods were used to achieve the goals of the ethics curriculum.

Morning Report Conference

On a monthly basis, the author engaged the residents (approximately 15–20) in a 1-hour discussion on medical ethics issues, using one of the following teaching methods:

Case method. Predetermined cases that highlighted specific ethical issues (eg, cases from ethics committee files or publicized court cases such as *in re Conroy,* 98 NJ 321 486 A 2d 1209 [1985] and *Cruzan v Director, Missouri Department of Health,* 110 S Ct 2841 [1990]) were used to stimulate discussions. Cases were selected ahead of time, and active discussion was encouraged. Topics discussed at these sessions have included concepts, policy, and practical issues related to advance directives, surrogate decision making for incompetent patients, competency assessment, brain death, assisted suicide, and forgoing of life-sustaining treatments.

Journal Club. Articles from medical journals were also used as triggers for discussions. The journal club discussions were frequently led by residents taking the ethics elective. The distribution of medical ethics articles obtained from prestigious medical journals (eg, the *New England Journal of Medicine*) may promote the perception that discussion of ethical issues is important. Topics and associated articles reviewed have included the costs of administering "futile" treatments,[7] disability determination,[8] the notion of noncompliance,[9] and rationing.[10]

Videos. Discussions on managed care were triggered by viewing segments from the video *Your Money and Your Life.*[11] Other videos being considered include *WHOSE Death Is It, Anyway?*[12] and segments from popular television shows (eg, *Chicago Hope*).

Literature. Short literary pieces were selected that could be read by the group at the beginning of the session. Literary methods are considered useful in medical ethics education.[6,13,14] Reading literature can enhance the realization that patients have "narrative" lives, and that every patient encounter represents a singular event situated within a more complex contextual structure (encompassing plot, motives, and characterization). One hopes that consequently, physicians may listen more fully to a patient's narrative of illness. Reading literature, especially when performed within a group of people, also may enhance flexibility of perspective by increasing awareness of the many different interpretations that can be attached to the same text. Literary pieces that have been interpreted at the morning report sessions include *The Use of Force* by William Carlos Williams,[15] *An Infected Heart* by John Stone,[16] and *What the Doctor Said* by Raymond Carver.[17]

Writing exercises. At morning report, residents have been asked to write on one of the following topics: *1*) my most memorable 3 AM wake-up call, *2*) a patient who had an influence on me, or *3*) my most repulsive patient. When physicians write about their patients, they begin to feel what their patients feel, which fosters empathy.[18] Furthermore, writing allows physicians to gain access to

TABLE 1.—*Ethical Issues Raised Most Frequently on Ethics Ward Rounds**

Withdrawal and withholding of life-sustaining treatments
Administration of resources considered futile, especially CPR
Competency of patients who are refusing therapy
Patients/families demanding treatments that physicians do not advise
Dealing with abusive patients
Dealing with patients who are noncompliant with the medical regimen (eg, patients who continue to smoke or leave the hospital to obtain illegal drugs)
The obligation of the medical profession to care for patients with "unhealthy" lifestyles (ie, the ethics of patient responsibility)
Surrogate decision making

*Issues are listed in order of decreasing frequency.
CPR = cardiopulmonary resuscitation

inarticulated feelings, presenting an opportunity for them to create some sense of connection between their "professional" and "personal" selves.[19] When residents share their writings and compare their experiences and feelings with one another, benefits similar to those realized within a support-group setting are achieved.

Monthly Ethics Ward Rounds

Every month the author visited each of the medical services (general medical wards, coronary care unit, and medical intensive care unit) to conduct ethics ward rounds with the residents, interns, and medical students. The senior resident on the service selected a patient from the ward whose situation was thought to contain an ethical dilemma. This teaching format lends itself to two types of pedagogical methods:

Case discussions. After a patient was presented, a discussion occurred concerning the ethical dimensions of the case. Issues that have been raised most often (70%) are shown in Table 1 and are listed in order of decreasing frequency. Other issues brought forth from the selected cases, but on a less frequent basis, are shown in Table 2.

Discussing ongoing dilemmas probably stimulated residents' interest more than the predetermined cases used at the morning report sessions. The active selection of cases by the residents seems to have enhanced their ability to recognize and appreciate the ethical dimensions of medical practice. Initially, when residents were asked to select cases for discussions, they expressed doubt as to whether there were patients whose situations contained an ethical issue. After a year of experiencing ethics ward rounds, however, they no longer expressed such skepticism, and usually presented several cases.

Role playing. Discussions of cases offered role-playing opportunities on such topics as speaking about code status and giving "bad" news. Such role-playing exercises can help to improve interaction skills.[1,4]

Ethics Elective

Residents had the option of taking this elective for either 2 or 4 weeks. They pursued the following activities: *1*) focused readings on selected issues and subsequent discussions with the course mentor and other residents taking the elective, *2*) participation in the

TABLE 2.—*Ethical Issues Raised Less Frequently on Ethics Ward Rounds*

Confidentiality issues (eg, a patient with AIDS who is a hospital employee)
Informed consent (eg, the ethics of obtaining CD4 counts without patient consent)
Informed consent in research trials (eg, the ethics of obtaining consent when the physician and the investigator are the same person)
Family requests that patients not be told of their diagnosis
The subjectivity of selection criteria for organ transplantation
Criteria for disability and the obligation of housestaff physicians to make this determination
Conflicts between housestaff and attending physicians on management issues
The inconsistency with patients desiring CPR and refusing other diagnostic tests and procedures
Patients going to the emergency room with the intent of obtaining a central line to inject illicit drugs
Spouse is not coping with wife's illness and hence making it difficult for the staff to care for the wife and other patients on the ward
Managed care issues (eg, the ethics of transfers to satisfy previous economic arrangements)
The extent of physician bias and prejudices in treatment of patients
Family coercion involved with a patient's decision to go to a nursing home
The scope of physician advocacy for patients

AIDS = acquired immunodeficiency syndrome

ethics ward rounds, *3*) attendance at the main meeting of the hospital ethics committee, *4*) attendance at ethics seminars occurring at the medical center, and *5*) participation in ethics consults. Concerning the latter, residents would be involved in any consult performed by the hospital's Ethics Consultative Service, thus having the opportunity to witness how ongoing ethical dilemmas are analyzed within an ethical framework in an attempt to achieve consensus among all participants.

Discussion

This paper has described an attempt to weave an ethics curriculum into the confining structure of a residency program. The described curriculum, consisting of case discussions, literary readings, videos, role playing, and writing exercises, differs from other reported curricula in that a specific block of time was not available whereby residents could be exposed to a core curriculum provided by didactic lectures.[3,20] The essentialness of didactic lectures remains unclear. Several studies have demonstrated the effectiveness of formal ethics courses in enhancing knowledge and attitudes.[21,22] A study comparing an ethics education program consisting of a lecture series with a program consisting of lectures and case conferences, however, observed no difference between the two groups in the amount of knowledge gained or attitudes developed about selected ethics issues.[20]

Future directions of the described curriculum include more focus on issues that affect residents on a more personal level. These are probably similar to those described for medical students[23] and include *1*) conflicts engendered by a desire to be a team player, *2*) questioning the authority of attending physicians without fear of retribution, *3*) how to deal with the witnessing of unethical behaviors, *4*) how to challenge medical routine, and *5*) how to balance one's professional and personal lives. Another area of focus would be the exploration of issues relevant to the ambulatory setting (eg, the role of physicians as gatekeepers and informed consent for screening tests).

The implementation of ethics education in a residency training program is expected to affect the knowledge, attitudes, and behavior of residents. The experience gained in the program described in this paper may assist other residency programs in their attempts to introduce medical ethics education into their curricula.

Acknowledgments

The author would like to express his thanks to Dr John A. Kastor, past chairman of the University of Maryland Department of Medicine, and Dr Susan Wolfsthal, director of the University of Maryland Residency Program, individuals whose support and encouragement made the implementation of the ethics program a reality.

REFERENCES

1. Fox E, Arnold RM, Brody B. Medical ethics education: past, present, and future. Acad Med 1995; 70:761–769

2. Residency Review Committee for Internal Medicine, Accreditation Council for Graduate Medical Education. Revised Special Requirements for Residency Training Programs in Medicine. Chicago, IL, ACGME, 1993, pp 10–11

3. Arnold RM, Forrow L, Wartman SA, Teno J. Teaching clinical medical ethics: a model programme for primary care residency. J Med Ethics 1998; 14:91–96

4. Povar GJ, Keith KJ. The teaching of liberal arts in internal medicine residency training. J Med Educ 1984; 59:714–721

5. Barnard D. Making a place for the humanities in residency education. Acad Med 1994; 69:628–630

6. Hunter KM, Charon R, Coulehan JL. The study of literature in medical education. Acad Med 1995; 170:787–794

7. Teno JM, Murphy D, Lynn J, et al. Prognosis-based futility guidelines: does anyone win? Am Geriatr Soc 1994; 42:1202–1207

8. Shaner A, Eckman TA, Roberts LJ, et al. Disability income, cocaine use, and repeated hospitalization among schizophrenic cocaine abusers. N Engl J Med 1995; 333:777–783

9. Orentlicher D. Denying treatment to the noncompliant patient. JAMA 1991; 265:1579–1582

10. Hadorn DC. Setting health care priorities in Oregon. JAMA 1991; 265:2218–2225

11. Your Money and Your Life: America's Managed Care Revolution [videotape]. A Fred Friendly Seminar. New York, NY, Seminars Inc, 1995

12. WHOSE Death Is It, Anyway? [videotape] New York, NY, Choice in Dying Inc, 1996

13. Charon R, Banks JT, Connelly JE, et al. Literature and medicine: contributions to clinical practice. Ann Intern Med 1995; 122:599–606

14. Hunter KM. Doctors' Stories: The Narrative Structure of Clinical Knowledge. Princeton, NJ, Princeton University Press, 1991

15. Williams WC. The use of force. In Reynolds R, Stone J (Eds). On Doctoring: Stories, Poems, Essays. New York, NY, Simon & Schuster, 1995, pp 89–92

16. Stone J. An infected heart. In Mukand J (Ed). Vital Lines: Contemporary Fiction About Medicine. New York, NY, St Martin's Press, 1990, pp 80–83

17. Carver R. What the doctor said. In Reynolds R, Stone J (Eds). On Doctoring: Stories, Poems, Essays. New York, NY, Simon & Schuster, 1995, p 360

18. Charon R. The narrative road to empathy. In Spiro H, Curnen MGM, Peschel E, St James D, (Eds). Empathy and the Practice of Medicine. New Haven, CT, Yale University Press, 1993, pp 147–159

19. Welch K. Narrative Writing: A Reflective Medium from The Center, Hiram, OH, Hiram College, July, 1996.

20. Sulmasy DP, Geller G, Levine DM, Faden RR. A randomized trial of ethics education for medical house officers. J Med Ethics 1993; 19:157–163

21. Givner N, Hynes K. An investigation of change in medical students' ethical thinking. Med Educ 1983; 17:3–7

22. Seigler M, Rezler AG, Connell KJ. Using simulated case studies to evaluate a clinical ethics course for junior students. J Med Educ 1982; 57:380–385

23. Christakis DA, Feudtner C. Ethics in a short white coat: the ethical dilemmas that medical students confront. Acad Med 1993 68:249–254

Editorials

The Problem of Methamphetamine Toxicity

THE TWO ARTICLES on methamphetamine in this issue draw attention to an important fact: We know very little about this drug. Most of what we do know comes from the Japanese literature and a handful of published case reports. But generalizing from case reports is unreliable, and the experience of other cultures may not apply to ours. Methamphetamine has been a major problem in Japan since the end of World War II,[1] but in the United States the overall prevalence of methamphetamine misuse has remained modest, especially when compared to cocaine.

In the 1996 report of the Drug Abuse Warning Network (DAWN), 4,462 deaths were attributed to cocaine compared to only 487 for methamphetamine, roughly a 10 to 1 ratio.[2] Preliminary results for 1997 suggest little change. Emergency room visits have nearly doubled, however, from the first half of 1996 to the first half of 1997 (from 4,200 to 8,400). There were 80,000 cocaine-related visits during that same period.[3] Unlike cocaine, which is a major problem everywhere in this country, methamphetamine misuse remains less common. Since 1991, not a single death from methamphetamine misuse has been reported in Atlanta, Baltimore, Boston, Buffalo, Miami, or Newark.

The demographics of this drug raise some fascinating questions about mechanisms of toxicity. DAWN statistics for 1997 indicate that more than half the emergency room visits were by people under age 35 (4,482/8,316) and that a third of the visits to emergency rooms due to methamphetamine misuse were by women (2,983/8,316). In autopsy studies, however, the mean age of decedents is closer to 38 years, many are in their 40s and 50s, and almost all are men. This is consistent with the results of successive National Household Surveys on drug misuse. That instrument continues to show that the population of drug misusers is aging. In 1979, when the survey first began, only 10% of misusers were over age 35. The percentage has now increased to nearly a third.[4] This age disparity raises the possibility that methamphetamine-related deaths may have a long incubation period. Typical findings at autopsy include multivessel coronary artery disease and myocardial hypertrophy.[5] Aortic dissection is also more common than is generally appreciated. Multivessel coronary artery disease does not develop overnight, and neither does myocardial hypertrophy or medial degeneration. The evidence suggests that most methamphetamine users die of chronic, not acute, toxicity. The full extent of the problem may not be apparent for several more years.

Today, most journal editors would reject a paper on myocardial infarction related to cocaine misuse on the grounds that the disorder is so common that it is no longer reportable. Yet only a handful of reports describe infarction in methamphetamine misusers. The explanation may have to do with the production of heat-shock protein. In experimental animals, amphetamines can increase levels of the inducible heat-shock proteins. These are a group of cellular homeostatic proteins induced in vascular tissue by catecholamines.[6] Cocaine does not appear to be as effective an inducer of heat-shock protein as methamphetamine. It may be that methamphetamine misusers benefit from a degree of myocardial protection that cocaine misusers do not.

Many other questions remain to be answered; but because complications from methamphetamine misuse are uncommon, these answers will be hard to come by. Environmental exposure to drugs is a reality. Cocaine, for example, can be detected in most circulating currency.[7] A few years ago, in California, a mother was charged with murder by breast feeding when a few nanograms of methamphetamine where detected in her dead son. The child also had viral pneumonia and pericarditis.[8] The detection of trace quantities of a drug only proves that the drug is in the environment, not that it has caused any particular syndrome. Even very substantial amounts of drug may represent nothing more than an incidental finding.[9] Great care must be taken not to needlessly exaggerate the threat by extrapolating too much from isolated case reports.

STEVEN KARCH, MD
Assistant Medical Examiner
City and County of San Francisco
San Francisco, California

REFERENCES

1. Suwaki H. Methamphetamine abuse in Japan. NIDA Res Monogr 1991; 115:84–98

2. Substance Abuse and Mental Health Services Administration. Drug Abuse Warning Network, Annual Medical Examiner Data 1996. Rockville, MD, Substance Abuse and Mental Health Services Administration, 1998

3. Substance Abuse and Mental Health Services Administration. Mid-year 1997 preliminary emergency department data from the Drug Abuse Warning Network. Rockville, MD, Substance Abuse and Mental Health Services Administration, Office of Applied Statistics, 1998

4. Substance Abuse and Mental Health Services Administration. Preliminary results from the 1996 National Household Survey on Drug Abuse. Rockville, MD, Substance Abuse and Mental Health Services Administration, Office of Applied Statistics, 1998

5. Karch S, Stephens B, Ho C. Methamphetamine-related deaths in San Francisco: demographic, pathologic, and toxicologic profiles. J Forensic Sci 1999; 44:1–9

6. Salminen WF Jr, Voellmy R, Roberts SM. Protection against hepatotoxicity by a single dose of amphetamine: the potential role of heat shock protein induction. Toxicol Appl Pharmacol 1997; 147:247–258

7. Oyler J, Darwin WD, Cone EJ. Cocaine contamination of United States paper currency [published erratum appears in J Anal Toxicol. 1998; 22:15A]. J Anal Toxicol 1996; 20:213–216

8. Ariagno R, Karch SB, Middleberg R, Stephens BG, Valdes-Dapena M. Methamphetamine ingestion by a breast-feeding mother and her infant's death: People v Henderson [letter] [see comments]. JAMA 1995; 274:215

9. Karch SB, Stephens B, Ho CH. Relating cocaine blood concentrations to toxicity—an autopsy study of 99 cases. J Forensic Sci 1998; 43:41–45

Editorials

The JAMA Firing

THE CREDIBILITY OF medical journals took a beating in January 1999 when the editor of the *Journal of the American Medical Association* (JAMA) was fired by the journal's owner, the American Medical Association (AMA). The firing made it clear that medical journals are not always what they purport to be. Journals such as JAMA—and *The Western Journal of Medicine*—hold themselves out to practicing physicians as sources of information on the latest medical research, and present themselves to scientists as arbiters of quality in medical science. Yet apparently, the journals are also places of bias and outright censorship, where vested interests sometimes rule the day.

By now, the story of the JAMA dismissal is well known. Dr George Lundberg, editor of JAMA for 17 years, was fired for publishing a study about college students' thinking on sex.[1] The study, from Indiana University's Kinsey Institute, found that students don't think oral sex is the same thing as "having sex." The Kinsey data was collected back in the early 1990's, but had never been published. Last fall, when the Kinsey researchers sensed that their findings might have a special bearing on questions being raised about President Clinton, they submitted their article for publication to JAMA. JAMA sent it out for peer review. When it passed muster with the reviewers and editors, Lundberg pushed to have it appear in the journal sooner rather than later, using the mechanisms available for early publication.

Before the article was published, however, leaders at the AMA showed their disapproval. In science, commonly accepted methods for disagreeing with a published study include writing a letter to the editor, submitting an editorial to the journal, or undertaking research in order to demonstrate that the study findings cannot be reproduced. But AMA executives didn't take any of those steps. They own the journal, so they simply fired the editor. The AMA's CEO, Dr E. Ratcliffe Anderson, Jr, issued a statement noting, "It is not the AMA's business, nor is it JAMA's business—to interject itself into political controversy of this kind."[2]

Apparently, AMA leaders did not view the Kinsey findings as significant. They're entitled to their opinions, but physicians who take a sexual history as part of their standard history and physical might disagree. It is of interest to know that many patients won't mention oral sex unless it is specifically asked about. Dr Anderson may have been reflecting less on the study, per se, and more on the AMA and its desire for support from elected Republicans. Perhaps he wanted to dissociate the AMA from findings that could be used by pro-Clinton forces in the debate over impeachment.

Whatever Dr Anderson's intentions were, he took the wrong action. No medical editor should be fired for publishing an article. By doing so, the AMA has called into question the trustworthiness of all medical journals.

Physicians need to be able to trust someone to sort the wheat from the chaff in medical research. Typically, they've placed their faith in medical journals, because they know that journal articles are subjected to competitive peer review. Experts judge whether the quality of science in a given manuscript is up to snuff, and only a small minority of studies actually make it into print. Now, because of this firing, physicians must wonder every time they read a journal article: Was the article published on its merits, as high quality science? Or was the article published because the journal's owner concurred with its findings? These are very serious concerns. After he was fired, Lundberg acknowledged in an article in the *Chicago Tribune* (February 17, 1999) that in several instances while he was editor, he had faced substantial pressure, threats, intimidation and other attempts to influence the content and publication of articles in JAMA.

For the record, Dr Lundberg has a new job as editor of Medscape, a medical information service on the Internet. He claims he'll have editorial independence there.[3] Also for the record, the new owners of *The Western Journal of Medicine* have promised the new editors of this journal complete editorial freedom. It's a promise they don't make lightly. But if we had not been given such assurances, we would not be editing the journal.

MIRIAM SHUCHMAN, MD
Editor

REFERENCES

1. Sanders SA, Reinisch JM. Would you say you had sex if . . . .? JAMA 1999; 281:275–277

2. Anderson ER. American Medical Association statement; Chicago, IL, Jan 15, 1999

3. Fired editor of AMA journal takes new post. San Francisco Chronicle, Feb 25, 1999

Editorials

A Letter to the Executive Vice-President of the American Medical Association from Linda Hawes Clever

In response to the firing of Dr George Lundberg, Linda Hawes Clever communicates her thoughts and concerns to the AMA.

JANUARY 25, 1999

To: E. Ratcliffe Anderson, MD

Executive Vice-President and CEO
American Medical Association
515 N State Street
Chicago, IL 60610

Dear Dr. Anderson,

I am writing as a long-time member of the San Francisco Medical Society and the California Medical Association. I have been active in these organizations for years, chairing committees and task forces (most recently the Primary Care Task Force of the California Medical Association), attending board meetings (as guest and member), and recruiting new members. I also write as immediate past Editor of *The Western Journal of Medicine* and former Regent of the American College of Physicians.

My husband, also an internist, and I were out of the country when the first wave of news hit about your firing of George Lundberg, so perhaps we do not have the entire picture. I am also aware of the distortions that can take place in the press. Based on information available, however, I am compelled to ask the following questions:

- Why, really why, did you do this? I won't repeat others' hypotheses having to do with electoral politics and attitude. Perhaps it is the old-fashioned "hubris" that the Greeks described so well.
- How do you plan to maintain morale within the fine JAMA staff?
- How do you think you will ever recruit a distinguished successor, given the nature of Dr. Lundberg's departure?
- Do you have any idea of the ever-deepening well of disrespect that you are digging for the AMA? William Osler said, "Do the kind thing and do it first." Where does that philosophy fit in your management style? Public humiliation may be effective in some organizations, but not in medicine, a profession that depends on excellence, compassion, and good communications. Of course, you cannot humiliate Dr. Lundberg. His record and integrity stand strong and shining. You have humiliated the AMA. We expect leaders to act like doctors, not dictators.

Our country is going through dark hours. You have further darkened our profession's hours. I know you do not stand alone. The Board that was responsible for the Sunbeam situation is virtually the same Board as now. That Board is accountable for your actions. There will need to be new Board members, new administration, and abundant new vision. There will need to be a return to intellectual and publishing freedom before the public and profession can even start to regain its confidence in your organization. I am dismayed. Worse, really.

Sincerely,

LINDA HAWES CLEVER, MD, MACP
Chair, Department of Occupational Health
California Pacific Medical Center

Editorials

An "Old Timer" Reflects on the Use of the "Placebo Effect"

Sixty years ago, the term placebo was used interchangeably with "dummy pill" or "sugar pill." Since then, its meaning has undergone a gradual change. The application of the term placebo was broadened to include devices, procedures, and treatments. Now, the use of placebos has come to play a much more complex role in therapeutics. Placebos have been shown to result in physiologic and pathologic changes.[1,2] This has come to be known as the "placebo effect."

After a 50-year career in medicine, I now realize that the placebo effect is a powerful force that can play a significant role in therapy. Its success or failure depends heavily on these three conditions:

1) The patient has a preconditioned "faith" in the effectiveness of the "treatment" and the competence of the therapist.

2) The therapist has total conviction in and enthusiasm for the "theory" underlying the treatment, the correctness of the diagnosis, and the effectiveness of the treatment, and is able to communicate this conviction to the patient.

3) The therapy used plays into the patient's and the family's cultural concept of illness. The result of using a placebo is enhanced if treatment is accompanied by ceremonies and rituals performed by the therapist.

A patient's belief in spiritual, magical, or divine intervention is probably the most potent placebo enhancer. The more of these elements that are brought into play, the more powerful the placebo effect.

The placebo effect is not limited to drugs (pharmacologically active or nonactive). There is a saying among those familiar with back surgery that in many types of back pain, the results of a simple skin incision are as good as complex decompression and fusion procedures. (Think of the potency of the placebo effect of the surgical ritual!)[4]

Should such a powerful force be used by allopathic physicians? Some articles[1,3] suggest that if the "placebo effect" by itself can be shown to have a therapeutic benefit, then there is nothing wrong with using it! I agree, but only with qualifications. This is because the use of placebos challenges a physician's professional probity. As soon as a physician is totally upfront with patients ("I am going to give you a dummy pill and I have my doubts that you will be benefited by it"), much of the effectiveness of the placebo is defeated. Therein lies the paradox that confronts the physician.[5]

It is my opinion that the various "alternative medicine" disciplines, in contrast to "evidence-based allopathic medicine," utilize the placebo effect extensively; in fact, their success is largely built on the placebo effect, which I consider to be their stock-in-trade. By evidence-based allopathic medicine, I mean the kind of practice that has been validated by scientifically conducted and peer-reviewed studies.

Is the rising popularity of alternative disciplines a reaction by the public to what it perceives to be reluctance by the modern physician to employ the kind of placebos the public has come to expect?

Once can posit the following hypothesis:

Evidence-based therapy + placebo effect =
outcome experienced by patient

What then are we to do when a situation arises that seems to call for the use of the placebo effect? Should we refer the patient to a committed alternative-medicine practitioner down the street? Or should we use the placebo effect ourselves? Although our primary allegiance is to the scientific method, I suggest that it is acceptable for us to use the placebo effect provided there is no more than a negligible risk of harm and the cost of the "therapy" is insignificant. Here we are at a disadvantage! If we are true to scientific principles, and if we are not good actors and promoters, we would be hard-pressed to fulfill the second of the above list of conditions. Elaborate ritual can be expensive, creating a conflict with the provision that the cost be insignificant.[6,7]

Nonetheless, we should not abdicate to others the utilization of the placebo effect where warranted. By virtue of our university medical education and postgraduate training, we are best positioned to understand the dynamics of illness and select optimum treatment—including the placebo effect—with the least chance of error or harm.[8]

Ultimately, we each have to assess our own comfort level with use of placebos to the patient's clinical advantage. In any event, to understand what we are doing, we physicians should pursue self-knowledge as well as medical expertise.

Acknowledgments

I thank Selma Cooperman, MD, PhD, and June E. Cooperman, MD, for their assistance; and Gloria Gilbreath for typing and editing.

REFERENCES

1. Straus JL, von Ammon Cavanaugh S. Placebo effects. Issues for clinical practice in psychiatry and medicine. Psychosomatics 1996; 37:315–326

2. Benson, H, McCallie DP Jr. Angina pectoris and the placebo effect. N Engl J Med 1979; 300:1424–1429

3. Weiner M, Weiner GJ. The kinetics and dynamics of responses to placebo. Clin Pharmacol Ther 1996; 60:247–254

4. Beecher HK. Surgery as placebo. JAMA 1961; 176:1102–1107

5. Brown WA. The placebo effect: should doctors be prescribing sugar pills? Sci Am 1998; 278:90–95

6. Bok S. The ethics of giving placebos. Sci Am 1974; 231:17–23

7. Brody H. The lie that heals; the ethics of giving placebos. Ann Inter Med 1982; 97:112–118

8. Oh VM. The placebo effect: can we use it better? BMJ 1994; 309:69–70

BERNARD COOPERMAN, MD,

Alban-Wertheimer Orthopaedic Group
Los Alamita, Califarnia

Commentary

Ash Wednesday

RICHARD R. PESCE, MD, *Chattanooga, Tennessee*

Entering the intensive care unit (ICU) to begin rounds after a weekend off call, I found a patient of mine had been admitted in respiratory distress. We had known each other since his coronary bypass surgery several months earlier. This surgery had been followed by multiple complications, including sternal breakdown due to staphylococcal infection. This was followed by four sternal repair attempts and finally omental flap closure before Drew could be weaned from the ventilator. The repairs were more difficult than usual because he had received radiation therapy to his mediastinal area for Hodgkin's disease many years before. This left him with a compromised blood supply to the sternum and a restrictive cardiomyopathy. After 2 months and many hours of worry on both sides, he could finally be discharged to home. He had been at the office a half dozen times since to control his pleural effusions by thoracentesis. The effusions finally began responding to combination diuretic therapy. The last time I saw him prior to admission he had improved and, although still weak, he was beginning to enjoy life and being with his family.

As I entered his ICU room I saw that things had quickly deteriorated. Staphylococcal endocarditis, acute and bacteremic, had taken hold. Drew looked gray, he was barely able to whisper, and his breath sounds were hardly audible.

"Drew, I have to help you breathe!"—he nodded in response. As we laid his head down for intubation he calmly submitted. I could not use any sedatives because of his hemodynamic instability. I needed to place an endotracheal tube and obtain venous access, but sternal surgery had caused contraction of his neck muscles, so no usual access was available. I continued, however, through radiation-toughened skin, and with care because his clavicles were out of alignment. I was able to obtain a femoral artery blood gas and place a femoral intravenous line. But I saw that this had caused him discomfort despite local anesthetic.

"My God," I thought. "I am taking part in a crucifixion." This man lay in front of me awake and suffering. I was unable to relieve his pain just then and had to continue to do procedures to stabilize him.

Drew's family had arrived, and quick exchanges took place. We had met many times before and had discussions regarding the "what ifs" of his condition. His family was wonderful and supportive. There was not anything they would not try to accomplish for their father and husband. His daughter asked if anything else could be done, knowing what the answer would be. (Even during his first surgery his aorta could not be cross-clamped because it was so friable. To attempt valve replacement was not possible.) As the patient's pressure continued to fall, episodes of bradycardia began. He would respond to boluses of epinephrine and then fade again. His wife asked that their priest be called to administer the Sacrament of the Sick and that comfort measures be taken.

They were. Father Mike arrived quickly. He had known this family for many years and had been in school with some of the children. As he began the service, Drew's family gathered at his bedside and prayed out loud the *Lord's Prayer*. Each person told Drew that he should feel free to go to his reward, thanking him for having loved and cared for them so well. As the priest continued the annointment, I could see the heart monitor record slower and slower beats. They all then kissed him goodbye. At the end of the last word of the last prayer the monitor became flatline. At 9:20 AM, it was over.

As the family said their last goodbye, each one thanked me for trying to help Drew. I was speechless. Seldom had I witnessed such closeness in a family, and seldom had I felt so powerless to do anything that may have been of benefit. Yet to have these people thank me was more than I could bear.

Later that morning, I attended the Ash Wednesday service at the hospital's chapel. Drew's family was there and Father Mike was saying the Mass. Ash Wednesday is the day most Christians begin to spiritually prepare themselves for the celebration of the death and resurrection of Christ on Easter Sunday. It culminates in the placement of ashes on the forehead to remind us that we are from the earth and shall return to it when we die. It is a time of sacrifice and reflection. I was the last person to receive the ashes. Father Mike looked at me and said, "From dust thou art and to dust thou shall return, Doctor."

(Pesce RR. Ash Wednesday. West J Med 1999; 170:237–238)

From the Chattanooga Heart Institute, 2501 Citico Avenue, Chattanooga, Tennessee.
Reprint requests to Richard R. Pesce, MD, 62 North Crest Road, Chattanooga, TN 37404.

As I acknowledged him, I thought, "Yes, I will accomplish this. But have I accomplished my mission 'To cure sometimes, alleviate suffering often, and comfort always'?" At that moment, Drew's wife approached me: "Thank you for always being there for us, you will always be in our prayers." At that moment my question was answered and doubt resolved.

On this Ash Wednesday, I felt the uplifting spirit of a family's love for their father and husband and the hope for a better life. I have been privileged. Thank you, Drew.

Commentary

Resuscitating Annie

MIKE DENNEY, MD, FACS, *Sausalito, California*

ResuscitAnne is a celebrity. As the original mannequin used to teach basic cardiopulmonary resuscitation (CPR) on television and in hospitals, schools, and community organizations, she is known to millions of people throughout the world. Annie has been rescued heroically from the abyss of death more than any other creature in human form, and thus she has become almost a mythic figure.

Annie and I have been soulmates. As a physician practicing CPR, I have shared with her the breath of life, spent many hours practicing with her the techniques for bringing the dead back to life, and shared our experience with others so that they, too, might learn the art. As I have participated as a student and a teacher in CPR over the years, I have observed that there is something hauntingly sensuous about the countenance of ResuscitAnne. Pondering that idea, I recently telephoned the Laerdal Medical Corporation in Stavanger, Norway, the place where the ResuscitAnne mannequin is manufactured. There, I discovered a most unusual story (T. Laerdal, CEO, Laerdal Corporation, oral communication, February 11, 1999).

Approximately 100 years ago, the lifeless body of a lovely young woman was pulled from the river Seine in Paris. Her identity never could be established and she came to be known only as the young woman from the river Seine. A death mask was made for legal purposes, and it was so beautiful that people bought reproductions. Stories about her were told again and again, and a kind of Victorian-era legend grew around her memory[1]—a legend of a shamed woman who committed suicide after being rejected by her lover. Sixty years later, a famous doll-maker, Asmund S. Laerdal, of Stavanger, Norway, was commissioned to create a lifelike mannequin to be used to teach CPR. Laerdal wanted his creation to be artistic, and he knew of the legend of the young woman from the river Seine. He thought it would be fitting to use her death-mask as the model for the mannequin's face. And so it is that the haunting face of our ResuscitAnne is, indeed, the face of the young woman from the river Seine.

Annie has changed dramatically in recent years, an example of modern science's triumph over art and symbol. For the efficient prevention of infectious diseases, Annie's once lifelike hair has been replaced with molded plastic, and her face and airway are now removable and disposable so as to be easily disinfected. For cost-effectiveness, her once full-length body, covered with clothing that was a replica of that worn by the drowned Parisian woman, has been replaced with just a bare torso, keeping only those parts that are needed for the exercise of CPR. As a result, Annie's lovely aura has been somewhat diminished.

Still, I wonder if there is a lesson in this story for those of us who practice modern medicine, in which science and technology has so often replaced soulful contact with patients. Might we in some way begin to bring spirituality into our practices if we imagine that when we perform CPR and mouth-to-mouth breathing on ResuscitAnne we gently kiss the young woman from the river Seine?

REFERENCE

1. Muschler RC. Die Unbekannte (a novel). Dresden, Germany, Wilhelm Heyne Verlag, 1936

(Denney M. Resuscitating Annie. West J Med 1999; 170:239)

Mike Denney is in private practice in Sausalito, California.
Reprint requests to Mike Denney, MD, PO Box 235, Sausalito, CA 94966.

Commentary

Confessions of a Beggarly Doctor

RALPH CRAWSHAW, MD, *Portland, Oregon*

I do not wish to be a welfare recipient, but I am one by act of Congress. Like other senior citizens signed up for Medicare, each time I see my doctor I become a charity patient, and I do not like it. Charity has at least two meanings: designating institutions designed to serve the poor, as in "charity organization"; or identifying the exchange of sentiments that accompany a benevolent act, as in President Lincoln's address, "With charity to all." Medicare, with much of the former and little of the latter, makes me a beggarly doctor.

My beggarly role does not arise from luckless deprivation since my career includes a remunerative practice of medicine. Short of catastrophe, I am prepared to pay my health care costs. Yet my health care insurer, Medicare, is determined to hold down its costs by setting medical fees below cost. Present Medicare reimbursement stints the quality of care for its patients by forcing a financial loss on many, very many, physicians.

My position stands in ironic contrast to those who, by circumstance, are forced to ask for charity yet are denied it because they are impoverished. But then all citizens must pay close heed to the crack of a federal bureaucratic whip, even as it drives us in ways we may not wish to go.

In questioning my role with the federal Medicare program, some may say I am ill informed or even wrong minded, since all that is involved is acting as claimant for governmental medical insurance. Oh, and what kind of insurance is it that holds the Samaritan responsible for paying for the victim's loss? Does fire insurance require the firefighter to pay for a portion of clean up and reconstruction of burned buildings? Does theft insurance expect the detective to pay for the thief's stolen booty? Yet, Medicare expects the steward of my medical care to make up any loss in treating me out of non-Medicare patients' pockets. Consequently, every time I have my eyes checked or an ache in my back diagnosed, I involuntarily become a Medicare charity patient.

There are those who might say, if you do not like it, simply drop your Medicare coverage and pay your own way. Such practical advice ignores my need for adequate financial protection against catastrophic illness, a circumstance that potentially could wipe away a lifetime of savings. My need is for protection against overwhelming loss, not a federal license to force my doctor to cover the cost of treating me.

The naive might wonder why I do not simply reimburse the short-fall out of pocket. FRAUD is the label federal authorities stamp on that arrangement. I know that from the physician side of Medicare. When the federal government learned that I had accepted the "Medicare" difference in question from a wealthy patient, I was promptly threatened with prosecution. After returning his money, I promptly severed professional ties with that insurance plan. Nor was canceling the contract an act of greed. Rather, it has proved much simpler to return to the classical approach of charging medical fees on a sliding scale, with adjustment to the patient's means, in some cases 10 dollars for an hour's psychotherapy.

But then, few practitioners can easily terminate their Medicare contracts. After 35 years of psychiatric practice without a paid staff, it takes relatively little income for me to cover the office rent, telephone bill, medical organization dues, and malpractice insurance. Additionally, my personal expenses grow less as the significant cost of college education for my children is done and the mortgage is paid, leaving sufficient savings to secure my wife's and my "future." In contrast, most practitioners I call upon for medical care maintain establishments requiring a significant income flow to pay for adequate office space; comprehensive malpractice insurance; and salaries of nurses, receptionists, and bookkeepers together with their retirement. Clearly, it makes no sense for my doctors to charge me below cost fees.

Like any patient, I do not wish my doctor to be distracted by concern with haste for moving on to a patient who will cover the loss of an enforced charity patient. Yet, I can not offer my physicians a penny beyond the mandatory 10 dollar co-pay. Should I suggest additional payment, I tempt fraud. Instead, I discovered a way that appears to restore a measure of financial balance to our patient-physician relationship, despite a third party peering over our shoulders. Preparing to leave, I ask the the name of my doctor's favored charity. Some responses are diffident, perhaps suspicious. Once home I send

(Crawshaw R. Confessions of a beggarly doctor. West J Med 1999; 170:240–241)

Ralph Crawshaw is in private practice in Portland, Oregon.
Reprint requests to Ralph Crawshaw, MD, 2525 NW Lovejoy, Portland, OR, 97210.

off a check to their charity for what I judge fulfills the real cost of caring for me.

Unsurprisingly, a sharp critic, returning to the Medicare issue, might say it is all well and good for me throw money around since I am a "rich" doctor, but what about the pensioner on the edge of destitution, facing mounting pharmaceutical bills? Certainly, it is folly to contribute financially to charity if tight for cash. But, on the other hand, who is so bereft of means and ability that they might not offer some service to a local charity in the name of their caring physician? Who can not spend an hour volunteering to help at the local United Way or, if house bound, telephoning neighbors to support a "Walk Against Cancer"? Who can not go the additional step to recognize their doctor struggles with a system that bleeds humanity from the patient/doctor relationship?

Aside from the initial shock my physicians may experience on learning they are dealing with a financially responsible senior citizen, the response has proved serendipitous. Notes of thanks come unbidden, while my medical care, which the small minded may label as tainted with bribe, has lifted an unwarranted beggarly status from my life.

I ask concerned senior citizens, does charity not flow two ways? Is it ever out of place to ask your doctor to name a charity? By leveling the ground beneath your medical care, you may accomplish healing wonders for both yourself and your doctor.

Correspondence

Death of a Truck Driver: Fatal Nicotinamide Poisoning Associated with Intravenous Drug Use

To The Editor: Street drugs are frequently adulterated by the vendor, a practice unbeknownst to the consumer. Adulterants may include toxic substances such as arsenic[1] and scopolamine.[2] We report a case in which the substitution of nicotinamide for a street drug resulted in a fatal poisoning.

A 42-year-old man was found dead in a truck parked at a rural New Mexico truckstop. A syringe, drug paraphernalia, vials, and a plastic bag containing clumped, granular, tan material were adjacent to his body. The man was an interstate truck driver who had previously stopped in Oklahoma and south Texas.

Autopsy demonstrated only one needle track, with fresh needle punctures over the extensor right wrist. Analysis of the granular tan material by gas chromatography–mass spectrometry (GC/MS) and of the syringe by thin-layer chromatography revealed nicotinamide and no other substances. A blood sample, also analyzed by GC/MS, contained 0.6 μmol/ml of nicotinamide. No ethanol or drugs of abuse were detected in the blood or urine. Insignificant amounts of lead, arsenic, and mercury were detected in the blood by atomic absorption. The blood was less than 5% saturated with carbon monoxide. Vitreous fluid electrolytes, creatinine, urea nitrogen, and glucose were normal. The cause of death was certified as nicotinamide poisoning.

We believe that in this case, nicotinamide falsely sold as a common street drug was purchased in the southwestern United States or in Mexico. Nicotinamide, a B-complex vitamin used to treat pellagra, has been substituted for crack cocaine[3] and methamphetamine,[4] but no adverse consequences have been recognized. With large oral doses (1–6 g) in human volunteers, blood concentrations of nicotinamide ranged from 0.7–1.1 μmol/ml.[5] In rats, subcutaneous administration of this substance in large doses caused respiratory depression, but blood nicotinamide concentrations were not reported.[6]

The mechanism of death in this case is unclear, but may be related to respiratory depression. Although a low concentration of nicotinamide was detected in postmortem blood, the dose and length of time between injection and death are unknown. Because it is possible that other individuals may use nicotinamide-adulterated drugs, physicians should consider nicotinamide poisoning in cases of suspected drug coma, especially when toxicologic analysis does not reveal common drugs of abuse.

KURT B. NOLTE, MD
Office of the Medical Investigator
University of New Mexico School of Medicine
Albuquerque, New Mexico
Medical Examiner/Coroner Information Sharing Program
National Center for Environmental Health
Centers for Disease Control and Prevention
Atlanta, Georgia

ROBERT B. PALMER, PHD
Toxicology Program, College of Pharmacy
University of New Mexico
Albuquerque, New Mexico

N. G. S. RAO, PHD
State of New Mexico
Scientific Laboratory Division
Toxicology Bureau
Albuquerque, New Mexico

REFERENCES

1. Lombard J, Levin IH, Weiner WJ. Arsenic intoxication in a cocaine abuser. N Engl J Med 1989; 320:869

2. Centers for Disease Control and Prevention. Scopolamine poisoning among heroin users—New York City, Newark, Philadelphia, and Baltimore, 1995 and 1996. MMWR Morb Mortal Wkly Rep 1996; 45:457–460

3. US Department of Justice–Drug Enforcement Administration. Simulated cocaine being sold in Wisconsin. Microgram 1996; 29:4

4. US Department of Justice–Drug Enforcement Administration. Microgram 1990; 23:1

5. Stratford MR, Rojas A, Hall DW, et al. Pharmacokinetics of nicotinamide and its effect on blood pressure, pulse, and body temperature in normal human volunteers. Radiother Oncol 1992; 25:37–42

6. Brazda FG, Coulson RA. Toxicity of nicotinic acid and some of its derivatives. Proc Soc Exp Biol Med 1946; 62:19–20

Correspondence

Biological Warfare

To The Editor: I read with great interest the article by Lesho et al,[1] as the history of biological warfare is one of my areas of particular interest. I noticed a few minor errors in their report, however, that I wish to correct here for your readership.

I am not aware of any reports of the intentional dissemination of variola (smallpox) through contaminated fomites occurring during the American Revolutionary War, although such actions had already proven the efficacy of this practice in the French and Indian War,[2–4] and could possibly have been repeated. In 1763, Sir Jeffrey Amherst, the commander of British forces in North America, wrote to Colonel Henry Bouquet, suggesting that it "be contrived to send the small pox among those disaffected tribes of Indians" threatening Fort Pitt in Pennsylvania. Even before their correspondence resulted in a deliberate and official plan, Captain Simeon Ecuyer, Fort Pitt's commander, reported a smallpox outbreak and had begun distributing contaminated blankets and handkerchiefs to the Native Americans.[2–4]

The second, but much more subtle error, is that the bacterial simulant dispersed in the New York City subway system in the 1960s was *Bacillus subtilis* var *globigii*,[2,4,5] not *B globi*. This was erroneously reported as *B globii* by Robertson[3] (referenced by Lesho et al) and a simple typographical or transcription error would result in *B globi*.

JEFFREY SUCHARD, MD
Department of Medical Toxicology
Good Samaritan Regional Medical
925 E. McDowell Rd, 2nd Floor
Phoenix, AZ 85006

REFERENCES

1. Lesho E, Dorsey D, Bunner D. Feces, dead horses, and fleas—evolution of the hostile use of biological agents. West J Med 1998; 168:512–516

2. Poupard JA, Miller LA. History of biological warfare: catapults to capsomeres. Ann NY Acad Sci 1992; 666:9–20

3. Robertson AG, Robertson LJ. From the asps to allegations: biological warfare in history. Mil Med 1995; 160:369–373

4. Christopher GW, Cieslak TJ, Pavlin JA, Eitzen EM. Biological warfare—a historical perspective. JAMA 1997; 278:412–418

5. Mobley JA. Biological warfare in the Twentieth Century: lessons from the past, challenges for the future. Mil Med 1995; 160:547–553

Classified Advertisements

The rate for each insertion is **$1.50 per word, with a 30 word ($45) minimum.** Confidential box number charge: $10 each month.
A word is defined as one or more letters bounded by spaces. The following gives some examples:

Michael S. Wilkes, MD	= 4 words	allergy/immunology	= 1 word
Send CV	= 2 words	Sacramento, CA 95817	= 3 words
A	= 1 word	804-979-8034	= 1 word
February 22, 1997	= 3 words		

Classified display rate $70 per inch. Maximum sizes: 1 column by 5" or 2 columns by 2" (2-1/8" per column). Larger classified ad space by special arrangements.
Copy for classified advertisements should be received not later than **first of the month preceding issue. All copy must be typed or printed.** Classified advertisers using Box Numbers forbid the disclosure of their identity; your inquiries in writing will be forwarded to Box Number advertisers. Although *The Western Journal of Medicine* believes the classified advertisements in these columns to be from reputable sources, we do not investigate the offers made and assume no liability concerning them. The right is reserved to reject, withdraw, or modify all classified advertising copy in conformity with the decisions of the Advertising Committee.

Please Type or Print Advertising Copy

Classified Advertisements Are Payable in Advance
CLASSIFIED ADVERTISEMENTS, THE WESTERN JOURNAL OF MEDICINE
P.O. BOX 7690, SAN FRANCISCO, CA 94120-7690
(415) 974-1071; FAX (415) 882-3379
Ads may be placed online at www.wjmed.com

GET IN THE SWIM

PHOTO PARADE / EDDIE ADAMS

If you know a child with muscular dystrophy who can benefit from a special getaway, tell him or her about MDA summer camps. They're fun and free!

MDA Muscular Dystrophy Association
1-800-572-1717 • www.mdausa.org

PHYSICIANS WANTED

California–Monterey Bay. Full/Part-time positions. 12 clinic urgent care System seeking BC/BE, EM/FP physicians. Work 2-3 days/week with 4-5 days off! Benefits include competitive compensation, malpractice insurance paid, 401k & health insurance. Practice in Californiaís most beautiful coastal recreational area. Contact Donaldo M. Hernandez, MD at 831-622-8400, Send CV to Medical Director, Doctors on Duty, 100 Clock Tower Pl., #220, Carmel, CA 93923, Fax to 831-622-8401 or Email to HYPERLINK mailto:mmcilla@doctorsonduty.com

California, Northern–Internist needed for 70+ physician group affiliated with Catholic Healthcare West. Hospital and office-based practice (50/50) with shared call, competitive income and comprehensive benefits. Contact Danise Cooper, 800-765-3055; ID#: 6400 WE; fax 314-726-3009; email: dcooper@cejka.com. Visit our website at www.cejka.com.

Salem/Willamette Valley–Salem Clinic, PC, a 40-physician multi-specialty group located in Salem, Oregon, is currently recruiting a full-time Internal Medicine physician. The position consists of a 4-day workweek. Salem Clinic offers a comprehensive benefit package and competitive income guarantee with opportunity for rapid incorporation into production formula. 1:7 call, single hospital town. If interested, please forward, fax or e-mail a copy of your CV to: Sherry Krog, Salem Clinic, PC, 2020 Capitol St. NE, Salem, OR, (503) 399-2470, Fax (503) 375-7429, e-mail HYPERLINK mailto:gunderBL@aol.com gunderBL@aol.com

EQUIPMENT FOR SALE

FOR SALE: BONE DENSITY EQUIPMENT (HOLOGIC 1000 PLUS). Pencil Beam, 4-years old, excellent condition. Central Dexa (Hip and Spine) and Periph (forearm). Best offer. Call 505-522-2626, ask for Jean.

MEETINGS/CONFERENCES

The 12th Annual Critical Care Cardiology Program. August 5-7, 1999. The Grand Hyatt San Francisco on Union Square, San Francisco, California. Sponsored by the American College of Cardiology. Program Directors: Kanu Chatterjee, MB, FRCP, FACC, and Thomas A. Ports, MD, FACC, 16.5 category 1 Credit hours. For information, call 800-253-4636, ext. 695, Fax 301-897-9745.

The ACC/SCA&I Board Review Program in Interventional Cardiology, August 26-29, 1999, Hyatt Regency San Francisco (Embarcadero), San Francisco, California. Sponsored by the American College of Cardiology, and the Society for Cardiac Angiography and Interventions. Program Directors: George W. Vetrovec, MD, FACC, FSCAI, and Morton J. Kern, MD, FACC, FSCAI, 21 category 1 credit hours. For information, call 800-253-4636, ext. 695, Fax 301-897-9745.

Western Journal of Medicine

INSTRUCTIONS FOR AUTHORS

In accordance with the Uniform Requirements for Manuscripts Submitted to Biomedical Journals (URM), 1997

Our readers represent all branches of medicine. We aim to publish manuscripts that are reliable and lively and that will improve the care of patients, the health of the public, or policies affecting either. Manuscripts should be of interest to a broad range of busy practitioners, physicians in training, and anyone who has an interest in health care. The purpose of a paper or letter may be to report, inform, alert, review, and discuss, but, above all, to teach. We aim to give quick and informative decisions on the articles we receive.

Manuscript Information

Manuscripts should be sent to the Managing Editor, Catherine Nancarrow, The Western Journal of Medicine, 221 Main Street, PO Box 7690, San Francisco, CA 94120-7690. Manuscripts must be original, not previously published, and not under consideration by another publisher. If preliminary data were included in another presentation or publication, this should be noted in the cover letter, and a copy of that publication should be included. Any conflict of interest, actual or potential, should be revealed to the Editors (see Letter of Transmittal). Obtaining informed consent to protect patients' rights to privacy should be documented according to URM 1997.

All manuscripts should be double-spaced and, including references and abstract but not tables, should not exceed:

- Original articles: 2,500 words with a maximum of five tables and 30 references
- Reviews: 1,500 to 2,000 words with a maximum of 25 references
- Topics in Primary Care Medicine: 2,000 words
- Evidence-Based Case Reports: 2,500 words with two tables and/or figures
- Commentaries: 600–800 words
- Letters to the Editor: 500 words

Manuscripts, except for Evidence-Based Case Reports, should include a structured abstract of no more than 250 words with the headings: objectives, design, setting, subjects, interventions, main outcome measures, results and conclusions.

Letters to the Editor must be double-spaced and will be published at the discretion of the Editors. They may be edited for style and brevity. Those of a scientific nature may be subject to peer review. They should be no more than 500 words in length.

All manuscripts will be subject to peer review in addition to review by the Editors to determine the originality, validity, and importance of content and conclusions. The WJM aims to introduce an open peer review system and reviewers' comments may be signed. Reviewers will be required to state possible conflicts of interest.

All accepted manuscripts are subject to copyediting, and the corresponding author is sent edited page proofs for approval and minor changes. It is the corresponding author's responsibility to clear all corrections and changes with coauthors.

Letter of Transmittal

All authors must sign the letter of transmittal, with one author designated as correspondent and his or her name, address, and telephone and fax numbers included.

The authors determine the order of authorship. All authors should meet the basic criteria for authorship (as stated below). Because the order of authorship is assigned in different ways, its meaning cannot be inferred accurately, unless it is stated by the authors. Authors may explain the order of authorship in a footnote.

A letter of transmittal, except for one accompanying a manuscript from US government employees whose work was done as part of their official duties, must include a paragraph that transfers copyright: "In consideration for reviewing and editing my submission, the author(s) undersigned hereby transfers, assigns, or otherwise conveys all copyright ownership to The Western Journal of Medicine, in the event that such work is published by the journal."

The letter of transmittal must include a statement of author responsibility signed by all authors: "I have participated in the conception and design of this work and in the writing of the manuscript and take public responsibility for it. I have reviewed the final version of the manuscript and approve it for publication. I attest to the validity and legitimacy of data in the manuscript and agree to be named as the lead author or coauthor of the manuscript."

The letter of transmittal must include a description of sources of funding and the role of sponsors, including their involvement, if any, in review and approval of the manuscript for publication. The letter must also include a statement of financial disclosure: "I warrant that I have no financial interest in the drugs, devices, or procedures described in the enclosed manuscript (except as disclosed in the attached statement)."

Research or project support should be included as a footnote to the manuscript or in the accompanying cover letter.

Manuscripts concerned with experimental investigation on human subjects must include in the text a statement that

all subjects gave their informed consent and that approval was obtained from the appropriate ethics committee.

Acknowledgments will be printed on a select basis to acknowledge those who contributed to but were not involved in the writing or review of the paper. They should not include persons whose work on the manuscript was a part of their regular duties.

Preparation of Manuscripts

Everything, including references, tables, figure legends, and abstracts, must be double-spaced.

Please submit the following: The original manuscript, two copies, and a copy of the manuscript on disk (formatted for a PC/Windows platform and labeled with the word processing program used). Allow a margin of 2.5 to 4 cm (1 to 1.5 in) on both sides. Be sure to include the references, tables, and figure legends on the disk. Formatting should be kept to a minimum. Manuscripts transmitted by facsimile machine are not acceptable unless requested by the Editors.

All values should be in Systeme International (SI) units, with metric equivalents following in parentheses. Temperature readings should be given in Celsius. Use the generic name of drugs, with the salt or ester given at the initial mention of a drug.

Figures should be submitted in triplicate in black and white, unmounted 12.7 × 17.8 cm (5 × 7 in) glossy prints, with the figure number, lead author's name, and top of the photo indicated with a label on the back.

The WJM encourages the use of illustrations and asks authors to submit photographs for publication. Patients should be asked to sign consent forms before pictures of them are published. This should be clearly stated and proof submitted with the manuscript. Changing the data on patients should not be used as a way of securing anonymity.

Figure legends, to be typed in sequence on the same page, should be in complete sentences. Any figures or tables previously published must be accompanied by a letter of permission to borrow from the copyright holder (the previous publisher). The permission of the authors should also be obtained. The Editors discourage the use of borrowed figures or tables.

Reprints

A form for ordering reprints will be sent to the corresponding author when the article is published.

References

All references should be cited in the text using superscript numbers and listed in their order of citation. The authors' names should be followed by the title of the article (abbreviated according to the style of Index Medicus), the year of publication, volume number, and first and last page numbers.

Journal Articles

Abbreviations of journal titles should conform to those used in Index Medicus. List up to three authors; for seven or more, use et al after listing the first three.

Vega KJ, Pina I, Krevsky B. Heart transplantation is associated with an increased risk for pancreatobiliary disease. Ann Intern Med 1996; 124:980–9832

Books

Author of book is same as author of chaper:

Ringsven MK, Bond D. Gerontology and Leadership Skills for Nurses. 2nd ed. Albany (NY). Delmar Publishers, 1996

Authors of book differ from chapter author:

Phillips SJ, Whisnant JP. Hypertension and stroke. In Laragh JH, Brenner BM (Eds). Hypertension: Pathophysiology, Diagnosis, and Management. 2nd ed. New York, Raven Press, 1995, pp 465–478

Correspondence

Shusterman D. Espresso maker's wrist [correspondence]. West J Med 1990; 152:721–722

Scientific or Technical Report

Issued by funding or sponsoring agency:

Smith P, Golladay K. Payment for durable medical equipment billed during skilled nursing facility stays. Final report. Dallas (TX): Dept of Health and Human Services (US), Office of Evaluation and Inspections; 1994 Oct. Report No.: HHSIGOEI69200860

Issued by performing agency:

Field MJ, Tranquada RE, Feasley JC, editors. Health services research: work force and educational issues. Washington DC: National Academy Press; 1995. Contract No.: AHCPR282942008

Sponsored by the Agency for Health Care Policy and Research. Centers for Disease Control and Prevention. Recommendations and Reports. 1997 Revised guidelines for performing $CD4^+$ T-cell determinations in persons infected with human immunodeficiency virus (HIV) MMWR Morb Mortal Wkly Rep 1997; 46(Jan 10):RR-2

Proceedings

Kimura J, Shibasaki H, editors. Recent advances in clinical neurophysiology. Proceedings of the 10th International Congress of EMG and Clinical Neurophysiology; 1995 Oct 15–19; Kyoto, Japan. Amsterdam: Elsevier; 1996

Mass Circulation Publications

Lee G. Hospitalizations tied to ozone pollution: study estimates 50,000 admissions annually. The Washington Post 1996 Jun 21; Sect A:3 (col 5)

Personal Communications and Unpublished Data

The use of "personal communication" or "unpublished data" should be avoided and should not be

included in the reference list. If such a notation provides essential information not available from a public source, it should be given in parentheses in the body of the text, listing the person's name, highest academic degrees, and professional affiliation, whether the communication was oral or written, and the date (month and year): Lyme disease has been reported in red squirrels (J. Sneed, PhD, Department of Wildlife, written communication, September 1990)

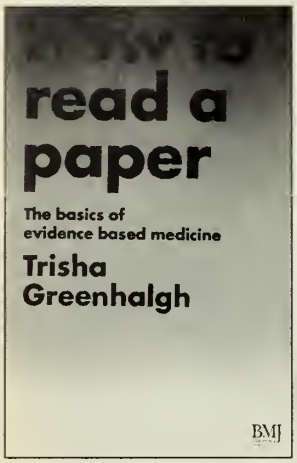
For Further Information

Questions regarding the Instructions for Authors may be directed to the Managing Editor in writing at the address above or by telephone (415) 974-5977, Fax (415) 882-3379.

AUTHOR CHECKLIST

- ✓ Original manuscript and two copies, as well as PC diskette.
- ✓ Everything double-spaced.
- ✓ Illustrations, black and white glossy, identified with lead author's name, plus figure legends that describe fully and in complete sentences what the figure depicts.
- ✓ Letter of transmittal that includes release of copyright, statement of conflict of interest, funding source(s), and authorship responsibility, signed by all the authors.
- ✓ A 250-word structured abstract.
- ✓ Title page that includes current affiliation of all authors and an address and telephone and fax number for corresponding author.
- ✓ Permission-to-borrow letters for any previously published illustrations or tables.
- ✓ Informed consent obtained.

Evidence based medicine...



How to Read a Paper

The Basics of Evidence Based Medicine
Trisha Greenhalgh
University College London, UK

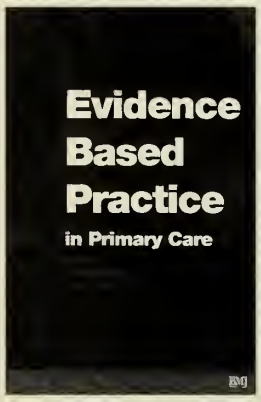
Written in a lively, jargon free style this best-selling book introduces the uninitiated reader to the principles of evidence based medicine and examines the criticisms levelled against it. The book covers such topics as literature searching, randomised controlled trials, and statistics for the non-statistician.

'An excellent book; it will reward those who study and apply its messages...it transmits the author's personality, enthusiasm, and sense of humour.' *David L Sackett*

'This clear and concise book provides an excellent starting point for those interested in finding their way through medical literature.' *Palliative Medicine*

$26.95

0 7279 1139 2 PB 216 x 138 mm 184 pp. 1997 (Login Book # H2426)



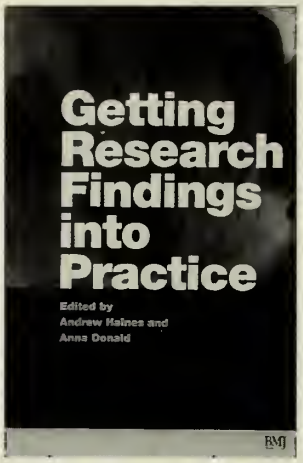
Evidence Based Practice in Primary Care

Edited by *Christopher Silagy*
Flinders University of South Australia
and *Andrew Haines*
Royal Free Hospital School of Medicine, London, UK

This guide is an introduction to those working in primary health care who have little or no knowledge of the theory and practice of evidence based medicine. The first section looks at the practicalities of applying EBM and its effect on decision making. The second section deals with the broader implications of EBM and how it affects professional practice internationally.

$45.00

0 7279 1210 0 PB 234 x 156 mm 208 pp. 1998 (Login Book # E0763)



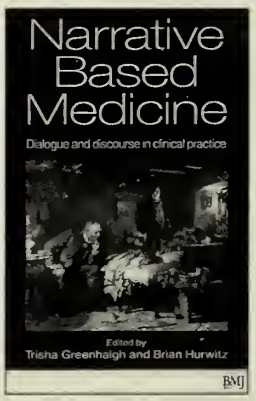
Getting Research Findings into Practice

Edited by *Andrew Haines*
Royal Free Hospital School of Medicine, London, UK
and *Anna Donald*
University College London, UK

Why is there such a wide gap between research findings and what actually happens in clinical practice? This accessible guide provides practical suggestions for implementing evidence based medicine in health care. Drawing together the key issues, with seminal chapters from leading thinkers, including: criteria for implementation; evidence based practice for providers; health economics; decision analysis; and closing the gap between research and practice.

$35.95

0 7279 1257 7 P8 216 x 138 mm 180 pp. 1998 (Login Book # H3221)



Narrative Based Medicine

Dialogue and Discourse in Clinical Practice
Edited by *Trisha Greenhalgh*
University College London, UK
and *Brian Hurwitz*
Imperial College School of Medicine, London, UK

The central theme of this book is the narrative nature of illness and the consequent need for interpretation as well as investigation of the patient's problem.

'A timely book, and one which is both stimulating and controversial. It will provide a fascinating read for many people. I defy anyone who reads 'The Conker Tree', or the patient based view of epilepsy, not to learn something.' *Kenneth Calman*

$35.95

0 7279 1223 2 PB 216 x 138 mm 304 pp. 1998 (Login Book # G3323)

BMJ Books are available from:

Login Brothers Book Company: Call: 888-858-7055 Fax: 800-339-1077 www.lb.com/bmj
1436 Randolph, Chicago, IL 60607 (Attn: Astralia/Donna) **and all good medical bookstores**

....from BMJ Books

Randomised Controlled Trials

Alejandro R Jadad
McMaster University, Canada

Written for anyone needing to understand RCTs, this readable handbook uses a question and answer format to explain all the basic information. Authored by an internationally known researcher from McMaster University, it provides a balanced view of the strengths and limitations of RCTs.

Contents include: RCTs: The basics; Types of RCTs; Assessing the quality of RCTs; Bias in RCTs; Reporting and interpreting individual trials; From trials to decisions: The basis of evidence based health care.

£23.50

0 7279 1208 9 P8 216 x 138 mm 128 pp. 1998 (Login Book # R2528)

Systematic Reviews

Edited by *Iain Chalmers*
Cochrane Centre, Oxford, UK
and *Douglas Altman*
Medical Statistics Laboratory, Imperial Cancer Research Fund, London, UK

A concise, ground-breaking book showing health care workers how to prepare a good review article and how to evaluate one.

'Attractively presented, highly readable, and packed with useful information.' *Journal of Clinical Nursing*

£26.95

0 7279 0904 5 P8 216 x 138 mm 128 pp. 1995 (Login Book # C1483)

The Pocket Guide to Critical Appraisal

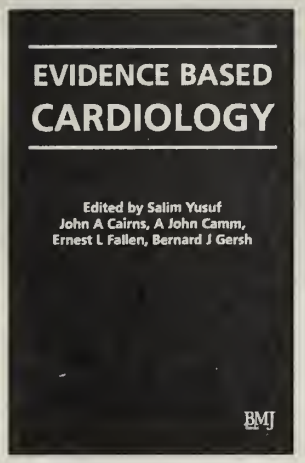
Iain K Crombie
Ninewells Hospital and Medical School, Dundee, UK

Everything you need to know to assess medical research is contained in this practical, accessible handbook. It provides a basic introduction to the principles and processes involved in critical appraisal, helping the researcher to make sense of the overwhelming mass of medical literature available.

'a brief well-written and entirely helpful guide.' *Family Practice*

£9.95

0 7279 1099 X PB 216 x 138 mm 80 pp. 1996 (Login Book # C2514)



Evidence Based Cardiology

Edited by *Salim Yusuf*
McMaster University, Ontario, Canada
***John Cairns*, University of British Columbia, Vancouver, Canada**
***John Camm*, St George's Hospital Medical School, London, UK**
Ernest Fallen*, McMaster University, Ontario, Canada and *Bernard Gersh
Georgetown University Medical Center, Washington, USA

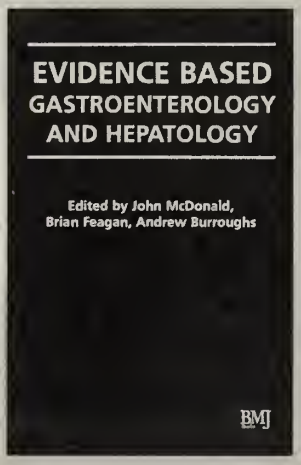
A ground-breaking text of major importance, addressing the implementation of evidence based medicine in the major cardiological subspecialties.

'Every physician and cardiologist should have a copy as a guide to the best treatment options for heart patients. Probably the most important publication in cardiological practice.' *Irish Medical Times*

$234.00

0 7279 1171 6 HB 260 x 190 mm 1200 pp. 1998 (Login Book # Y0289)

From April 1999 a free electronic update to the text will be available at www.evidbasedcardiol.com



Evidence Based Gastroenterology and Hepatology

Edited by *John McDonald* and *Brian Feagan*
London, Ontario, Canada
and *Andrew Burroughs*
Royal Free Hospital, London, UK

Edited by leading gastroenterologists working in evidence based medicine, this text recommends best practice for treating the individual patient based on the randomised controlled trials and systematic reviews conducted in the major gastrointestinal and hepatobiliary subspecialties.

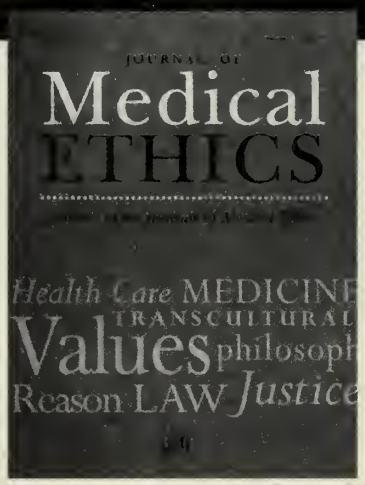
$117.00

0 7279 1182 1 H8 260 x 190 mm c.600 pp. July 1999
Introductory price until end of December 1999. (Login Book # M7201)

BMJ Books

Journal of Medical ETHICS

DOUBLE ISSUE - April '99



Announcing the April special issue...

Ethics and the new genetics

The April issue of the *Journal of Medical Ethics* will be a double issue of about 25 papers dedicated to the subject of ethics and the new genetics. The guest editors are Professor Bob Williamson and Associate Professor Julian Savulescu of the Murdoch Institute for Research into Birth Defects, Melbourne, Australia.

It will be of interest and benefit to a wide cross section of clinical and non-clinical professionals at a time of rapid and profound change in this area.

The issue comprises peer reviewed articles covering a wide range of issues: ethical problems raised by the prospect of human cloning, ethical and social issues around genetic screening and preimplantation genetic diagnosis, genetic testing in the wider arena of justice, and more.

Articles in this issue include:

- Should we clone human beings? Cloning as a source of tissue for transplantation
  Julian Savulescu and commentary by Bob Williamson
- Genetic screening with the DNA chip: a new Pandora's box?
  Wolfran Henn
- Beyond the disorder: one parent's reflection on genetic counselling
  Ruth Mc Gowan
- Preimplantation genetic diagnosis and the 'new' eugenics
  David King
- Does justice require genetic enhancement?
  Nils Holtung
- Genetic privacy: orthodoxy or oxymoron?
  Veronica English and Anne Sommerville

Individual copies are available to non-subscribers to the Journal of Medical Ethics from April '99. UK price £10 per copy including postage; overseas £12 per copy ($19 in the US) including postage.

Send orders to BMJ Publishing Group, PO Box 299, London WC1H 9TD, UK.
Tel +44 (0) 171 383 6270, Fax +44 (0) 171 383 6402, Email:subscriptions@bmjgroup.com.
Send US orders to: BMJ Publishing Group, Box 590A, Kennebunkport ME 04046, USA
Tel: 1-800-2-FON-BMJ Fax: 1-800-2-FAX-BMJ

BMJ Publishing Group

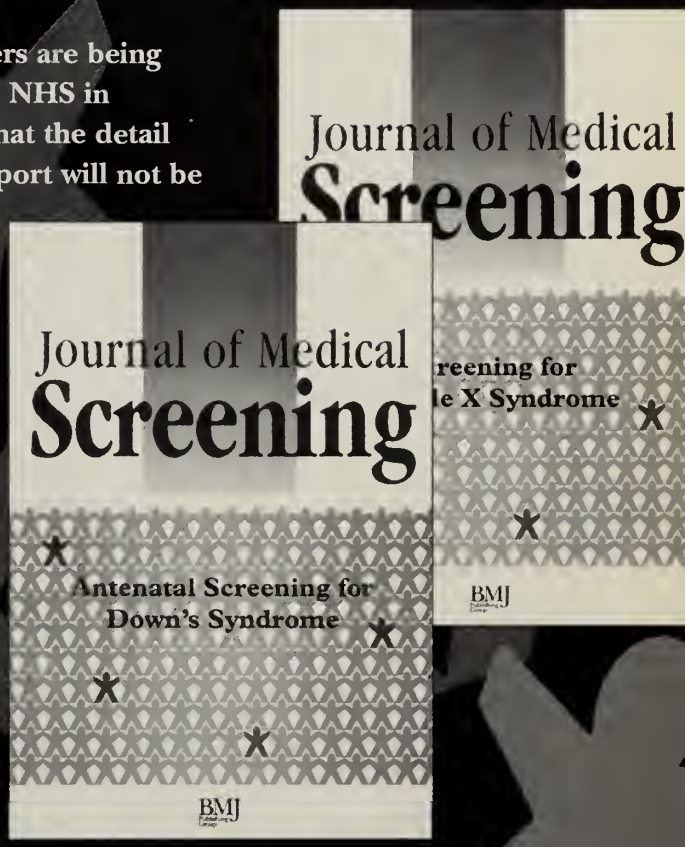
Systematic Reviews of SCREENING

Systematic reviews of screening for various disorders are being commissioned by health authorities, including the NHS in Britain. They are generally not published in full, so that the detail and the full list of references used to produce the report will not be made available.

Now available from BMJ are two full reviews, *Screening for Fragile X Syndrome* and *Antenatal Screening for Down's Syndrome*, published as special issues of Journal of Medical Screening.

Screening for Fragile X Syndrome aims at providing the information needed by health planners to judge whether or not to use DNA testing to screen for the disorder.

Antenatal Screening for Down's syndrome provides what is probably the most comprehensive and up to date summary of the subject that will be valuable to anyone involved in screening or responsible for making decisions on screening.



ORDER FORM

PLEASE SEND ME
Journal of Medical Screening:

- ☐ **Screening for Fragile X Syndrome**
- ☐ **Antenatal Screening for Down's Syndrome**

Price: £12.50/$21 USA only

☐ I enclose a cheque for .....(Payable to BMJ)

Sterling cheques to be drawn on a UK bank account.
US Dollar cheques to be drawn on a US bank account.

☐ Charge my credit card £/$.....

☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐

American Express/Visa/Mastercard/Delta/Switch
(delete as appropriate)

Issue No .....(Switch Cards only)

Expiry date .....Signature.....
(Your signature is essential when paying by credit card)

If your billing address differs from below, please advise us

Name .....

Specialty/Position .....

Address .....

.....

Country .....Postcode.....

☐ Please tick if you do not wish your data to be used for direct marketing purposes

Send orders to: BMJ Publishing Group, Journals Marketing Dept., PO Box 299, London WC1H 9TD, UK. Fax credit card orders to +44 (0)171 383 6402 Call our subscription hotline on +44 (0)171 383 6270 or BMJ Publishing Group, Box 590 A, Kennebunkport, ME 04046 USA. Tel 1-800-2-FON-BMJ Fax 1-800-2-FAX-BMJ

studentBMJ is an international monthly journal that contains similar features to the BMJ but for medical students.

studentBMJ covers subjects which matter the most to medical students everywhere.

subscriptions

To subscribe to the **studentBMJ** simply fill in the order form below. If you are a medical student in the UK you can receive the **studentBMJ** as a benefit of joining the British Medical Association (BMA).

articles & letters

Guidelines for authors are available from:
Student editor, **studentBMJ**, BMA House, Tavistock Square, London, WC1H 9JR, UK.

studentBMJ

The journal's **Education** section features articles written by experts who are asked to include the kind of information not normally found in textbooks - hints and tips that can take years of clinical experience to accumulate. Past features have included: • HIV and its Treatment • The uses of leeches in medicine • The risks of xray • Coping with surgery and loss of body parts.

The **Papers** section introduces the world of original scientific research giving medical students an insight into what lies ahead. Papers have included • Medical students attitudes towards complementary medicine • Association between alcohol and cancer

Life is where medical students write about the things that matter to them. Articles include • Heroin misuse • Community care in the South Pacific • Are you a gay medical student? • Anatomy lessons in Spain • Medical education in Brazil.

The journals **news and student politics** section reports on issues such as • Medical student debt • Drug misuse amongst students • Medical education • New advances in medicine.

As well as this there are editorials, personal views, reviews, letters and much, much more.

To receive a sample copy, simply complete the order form and return it to the stated address.

StudentBMJ Order Form

ISSN: 0966-6494 **Publication:** Monthly

1999 Subscription Rates These rates are valid from 1st January 1999 to 31st December 1999.

Personal Rate: £42.00 / US $68.00 **Institutional Rate:** £77.00 / US $123.00

Institutional rate applies to any library or organisation buying for the use of more than one person. US dollar rate applicable to USA subscribers only. Dollar payments must be drawn on a bank account in the USA. Sterling payments must be drawn on a bank account in the UK.

Please Tick
- ☐ Please send me a *FREE* sample copy
- ☐ Please enter my subscription starting from the month of .....
- ☐ I enclose a cheque for £/$ ..... *(Payable to British Medical Journal)*
- ☐ I wish to pay by credit card. £/$ .....

Personal Details (please complete in block capitals)

Name.....

Address .....

.....

Country .....Postcode.....

Email: .....

Please complete if applicable

I am studying at .....I am in year .....

Payment Details

Card Number ☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐

American Express / Visa / Mastercard / Delta / Switch *(Delete as appropriate)*

Expiry Date.....Switch issue number .....

Signature.....*(Your signature is essential, especially when paying by credit card.)*

If the credit card account holder's address differs, please advise.....

.....

.....

EC (non-UK) Customers will be charged VAT at the applicable UK rate, unless a VAT registration number is provided. Subscribers in the following areas please note: Italy and Spain must add 4% IVA, Ireland must add 21% VAT, France must add 20.6% TVA. Belgium must add 6% TVA/BTW, and Germany must add 7% MWS to the quoted sterling price. Canadian subscribers must add 7% GST.

☐ Please tick the box if you do not want your data to be used for direct marketing purposes

Please return the form to: BMJ Publishing Group, Student Subscription, PO BOX 299, London, WC1H 9TD, United Kingdom. Tel: +44(0)171 383 6270. Fax: +44(0)171 383 6402. Email: subscriptions@bmjgroup.com or BMJ Publishing Group, PO BOX 590 A, Kennebunkport, ME 04046, USA. Tel: +1-800-2-FON-BMJ. Fax: +1-800-2-FAX-BMJ. Email: bjpaige@cybertours.co

Visit the studentBMJ at: www.studentbmj.com

BMJ Publishing Group

wjm

western journal of medicine Volume 170 Number 5 May 199

DISPLAY SHELVES

Futility: Who decides when a life's not worth living?

How to take a sexual history

Why George D. Lundberg, MD, Chose to Join Medscape as Editor in Chief

The Web is revolutionizing access to healthcare information, and Medscape has set the standard of excellence in the medium. I am joining a team that is as passionate and dedicated as I am about improving healthcare by providing the highest-quality information possible. Medscape's authoritative Web site and its talented team of editors and executives were critical factors in my decision.

— George D. Lundberg, MD
formerly Editor of *JAMA* for 17 years;
Medscape member since 1996

Just point your Web browser to **www.medscape.com** and register for **free**. Then take advantage of the most comprehensive medical information (19 specialty sites), CME programs, Next Day Conference Summaries, Journals, Medscape Money & Medicine, and more!

Medscape®

www.medscape.com

This month in wjm

Women with recurrent cystitis may not benefit from further tests

At least one in 10 women will experience cystitis and 20% of these will suffer a recurrence. Recurrent bouts of cystitis are painful and irritating for women, who may become rapidly confused by conflicting treatment suggestions from both physicians and the media. On p.274 Lisa Chew and Stephan Fihn provide an evidence based guide to the management of this condition; how to prevent further infections with minimal adverse effects. There is little evidence that further investigations are useful for most women, but taking nitrofurantoin or a quinolone within two hours of sexual intercourse does reduce recurrence rates.

Who should decide when treatment stops?

Most people die in hospitals, so it's not uncommon for clinicians to make decisions about when treatment should stop. But what should happen when physicians feel patients cannot improve but families insist on more invasive treatment? On p.287, a working group from the Bay Area Network of Ethics Committees suggests a set of guidelines to resolve conflicts arising over futile medical treatment. On p.291, an author of a book on medical futility argues that such policies exist only for the physicians' benefit, and a lawyer warns that physicians may not be safe against malpractice suits. In Op-Ed on p.254, ethicist Charles Weijer claims that medical futility is a morally harmful concept.

Chinese herbal creams may contain steroids

Patients with eczema often report success with Chinese herbal creams. Keane et al (p.257) decided to analyze the content of creams used by their patients and found that most contained dexamethasone in various concentrations. The preparations were often supplied in unlabeled containers without clear instructions. The authors call for closer regulation of herbal medicines to ensure adequate labeling and to prevent dispensing of unlicensed products in the guise of herbal treatments.

New drug therapies may reduce radiographic signs of rheumatoid arthritis

Drug treatments for rheumatoid arthritis are usually aimed at relieving pain and inflammation. At least 2 million Americans suffer from this chronic and debilitating condition. In the past year new drugs have come on to the market that are aimed at reducing both symptoms and physical signs of the disease, and in Medicine Cabinet on p.278, Edgar R. Arriola and Nancy P. Lee discuss whether these drugs work, their side effects, and cost effectiveness. One drug, an immunomodulatory agent, is reported to reduce signs of erosions and loss of joint space on radiographs.

Taking a sexual history can cause embarrassment

Both physicians and patients can get embarrassed talking about sexual problems. In Toolbox on p.284, John Tomlinson and Etan C. Milgrom suggest how you can get patients to open up about sex, and how much you can learn from observing body language. They advise open ended questions rather than taking an accusatory tone, as in, "You've never been with a prostitute have you?"

Medical practice reflects social as much as scientific values

Lobotomies were once a popular treatment in psychiatry, although few would now argue that they work. Joel Braslow's examination of the historical records of Stockton Psychiatric Hospital on p.293 shows that most lobotomies were done for uncontrollable behavior, and the majority were carried out on women. There was no scientific rationale for this sexual discrimination. The operations were performed because they left patients docile and indifferent—personality traits thought to be more suited to women.

Jehovah's Witnesses don't all agree on refusing blood products

There are over 10 million Jehovah's Witnesses worldwide, many of them carrying the blood card that states they do not want to be given blood. But, as Osamu Muramoto points out on p.297, the religion bans some blood products while endorsing others. Plasma and platelets are forbidden on pain of exclusion from the religion, while stem cells and bone marrow are allowed. Not only are regulations increasingly complex as new blood technologies emerge, but some Jehovah's Witnesses have set up a reform group that supports the use of blood products by its adherents. Muramoto advises that physicians be sure to discuss blood products fully with their Jehovah's Witness patients.

THE FRANCIS A. COUNTWAY
LIBRARY OF MEDICINE
BOSTON, MA
JUN 07 1999

wjm

wjm western journal of medicine

221 Main Street, PO Box 7690, San Francisco, California 94120-7690

Co-editors:
Michael S Wilkes, Los Angeles, CA
mwilkes@ucla.edu

Miriam Shuchman, Buffalo, NY
shuchman@acsu.buffalo.edu

Deputy Editor:
Luisa Dillner, London, UK
ldillner@bmj.com

Editorial Manager:
Catherine Nancarrow
wjmsf@pacbell.net
Tel 415-974-5977
Fax 415-882-3379

Business & Marketing Manager:
Ruth Staunton
rstaunton@bmjgmup.com
Tel 415-974-1071
Fax 415-882-3379

Associate Editors:
David Grossman, Seattle, WA
Jerome Hoffman, Los Angeles, CA
Richard Kravitz, Davis, CA
John Takayama, San Francisco, CA

Section Editors

Medical Humanities
Janice L Willms, Santa Barbara, CA

Med.Pix
Richard Usatine, Los Angeles, CA

Evidence-Based Medicine
Nathan Link, New York, NY

Cultural Medicine
Geri Ann Galanti, Los Angeles, CA

eWJM
Doug Bell, Los Angeles, CA
Mark Granoff, Los Angeles, CA

Editorial Advisors
Elaine Batchlor, Oakland, CA
Joel Braslow, Los Angeles, CA
David Carlisle, Los Angeles, CA
Mitch Feldman, San Francisco, CA
Lillian Gelberg, Los Angeles, CA
Jan Gurley, San Francisco, CA
Seth Landefeld, San Francisco, CA
Gina Moreno-John, San Francisco, CA
Stephen McPhee, San Francisco, CA
Sylvia Ramos, Albuquerque, NM
Peter Rudd, Palo Alto, CA
Robert Tibshirani, Palo Alto, CA
Jeffrey Tice, San Francisco, CA
Howard Waitzkin, Albuquerque, NM
Mary White, San Francisco, CA

Editorial Board
Ann Alpers, San Francisco, CA
Margaret Battin, Salt Lake City, UT
William A Boehm, Alamogordo, NM
Rubin Bressler, Tucson, AZ
Robert Brook, Los Angeles, CA
Haile T Debas, San Francisco, CA
Thomas DeCoster, Albuquerque, NM
Albert Deisseroth, Houston, TX
Sandy Feldman, La Jolla, CA
Alan Fogelman, Los Angeles, CA
J Christian Gillin, San Diego, CA
Gary Glazer, Stanford, CA
John Greenlee, Salt Lake City, UT
John H Holbrook, Salt Lake City, UT
Philip Hopewell, San Francisco, CA
Vince Iacopino, Las Vegas, NV
Lewis Judd, La Jolla, CA
Norman Kahn, Kansas City, MO
Carol Lake, Sacramento, CA
Alex G Little, Las Vegas, NV
Jerold M Lowenstein, San Francisco, CA
Joseph L Lyon, Salt Lake City, UT
Julie G Madorsky, Pomona, CA
Michael L Manco-Johnson, Denver, CO
Daniel Mishell Jr, Los Angeles, CA
Albert A Moss, Seattle, WA
Thomas E Norris, Seattle, WA
George A Ojemann, Seattle, WA
Linda Rosenstock, Washington, DC
Paul Rousseau, Phoenix, AZ
Irwin J Schatz, Honolulu, Hawaii
Joe Schoeber, Casper, WY
Joe Selby, Oakland, CA
Martin Shapiro, Los Angeles, CA
Linda Shortliffe, Stanford, CA
Norman E Shumway, Stanford, CA
Anthony So, New York, NY
Reginald Strickland, Albuquerque, NM
Diane Wara, San Francisco, CA
Stephen I Wasserman, San Diego, CA
Ronald Weinstein, Tucson, AZ
Clifton R White Jr, Portland, OR
Leslie Wiener, Los Angeles, CA
Charles Wilson, San Francisco, CA

Submitting manuscripts
Send manuscripts to Catherine Nancarrow at the above address. Instructions for authors are published in the May 1999 issue and are available on request.

Subscriptions
To order your subscription, contact Jennifer Paige
WJM, Box 590A,
Kennebunkport ME 04046;
Tel 800-236-6265
Fax 800-232-9265
E-mail bjpaige@cybertours.com

1999 Subscription rates:
Regular rate $70 US/Canada;
$85 Other
Institutional rate $120 US/Canada;
$130 Other
Student, Group and Association rates available on request
Single copies $15 US/Canada

Display advertising and reprints
Contact Marsha Fogler
Medical Reprint Services,
PO Box 3227,
Cherry Hill, NJ 08034;
Tel 800-482-1450
Fax 609-482-7414
E-mail fogler@erols.com

Advertisements: Artwork for display advertising must be received no later than the first of the month preceding issue. Advertising rates will be sent on request. Acceptance of advertising is contingent upon approval by the Publisher. WJM reserves the right to refuse any advertisement.

Classified advertising
Contact Ruth Staunton at WJM Western Journal of Medicine, 221 Main Street, PO Box 7690, San Francisco, CA 94120-7690; tel 415-974-1071; fax 415-882-3379; e-mail rstaunton@bmjgroup.com

WJM Western Journal of Medicine
(ISSN 0093 0415/USPS 084 480)
is published monthly by BMJ Publishing Inc., 221 Main Street, PO Box 7690, San Francisco, CA 94120-7690.

Copyright © BMJ Publishing Inc. 1999. All Rights Reserved.

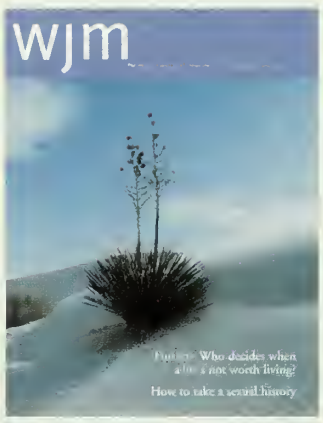
Periodicals postage paid at San Francisco, CA and additional mailing offices.

BMJ Publishing Group

UCSF STANFORD HEALTH CARE

WJM is owned by BMJ Publishing Group and UCSF Stanford Health Care.

WJM is the official journal of the following medical associations: Alaska, Arizona, California, Denver, Idaho, Nevada, New Mexico, Utah, Washington, and Wyoming



May 1999

Yucca plant as seen in White Sands National Monument, New Mexico

Op-Ed

252 To our readers
Michael S Wilkes, Miriam Shuchman

253 Rethinking case reports
Jerome R Hoffman

254 Medical futility
Charles Weijer

Mail

255 The power of herbs
Paul Gahlinger

256 A warm welcome
Western Medical Associations

Original Research

257 Analysis of Chinese herbal creams prescribed for dermatological conditions
FM Keane, SE Munn, AWP du Vivier, EM Higgins, NF Taylor

259 Commentary
Stephen Bent

260 Historical cohort study of in utero exposure to uterotonic drugs and cognitive function in young adult life
Henrik Toft Sørenson, Flemming Hald Steffensen, Svend Sabroe, Kenneth J Rothman, Matthew W Gillman, Peer Fischer

262 Commentary
Kristin Yaffe, Sumner J Yaffe

Med.Pix

263 Herpes zoster distribution—a lesson in anatomy
Richard P Usatine, Carmine Clemente

contents wjm

Volume 170 Number 5 MAY 1999

Research Digest

264 Does regular exercise during pregnancy affect the physical growth or mental development of infants?
JF Clapp 3rd, S Simonian, B Lopez, S Appleby-Wineberg, R Harcar-Sevcik

264 Commentary
Grace Edwards

265 Are baseline depressive symptoms associated with smoking initiation in adolescents?
LG Escobedo, M Reddy, GA Giovino

265 Commentary
Naomi Breslau

266 Self-management education for adults with asthma improves health outcomes
PG Gibson, J Coughlan, M Abramson, et al

266 Commentary
Peter K Honig

267 Older adolescents discuss sexual behavior with partners after trust has been built
SE Lock, SL Ferguson, C Wise

267 Commentary
Lynn Rew

Best Practice

268 Evidence-Based Case Review
Heart failure: Part I. First hospitalization and post-hospital care
Michael S Wilkes, Holly Middlekauff, Jerome R Hoffman

274 Clinical Evidence
Recurrent cystitis in nonpregnant women
Lisa D Chew, Stephan D Fihn

278 Medicine Cabinet
Treatment advances in rheumatoid arthritis
Edgar Arriola, Nancy P Lee

282 Curbside Consult
Is bungee jumping safe?
Craig Young

What advice can I give my patients with lymphedema?
Sylvia M Ramos

Why do people yawn?
Anita K Simonds

284 Toolbox
Taking a sexual history
John Tomlinson, Etan C Milgrom

Sean Ellis/Tony Stone Images

Culture and Medicine

287 Nonbeneficial or futile medical treatment: conflict resolution guidelines for the San Francisco Bay Area
Bay Area Network of Ethics Committees (BANEC) Nonbeneficial Treatment Working Group

291 Commentaries
Susan B Rubin
Ann Alpers

293 Therapeutic effectiveness and social context: the case of lobotomy in a California state hospital, 1947-1954
Joel Braslow

297 Recent developments in medical care of Jehovah's Witnesses
Osamu Muramoto

In The Public Eye

302 Media Watch
Deborah Josefson

304 News and Features

West of the Rockies

307 Speaker's Corner
A memorable incident: when a shovel should be an agricultural implement
PJ Tomlin

308 Letter from the Northwest
From academia to private medicine: where did the profession go?
John Roberts

309 *New Encyclopedia of the American West* by Howard Lamar
Book Review by Ralph Crawshaw

310 Poets and Healers
Essay by Janice Willms

310 Fire Shadows
Poetry by Gwen Head

313 Classified Ads

314 CME Announcements

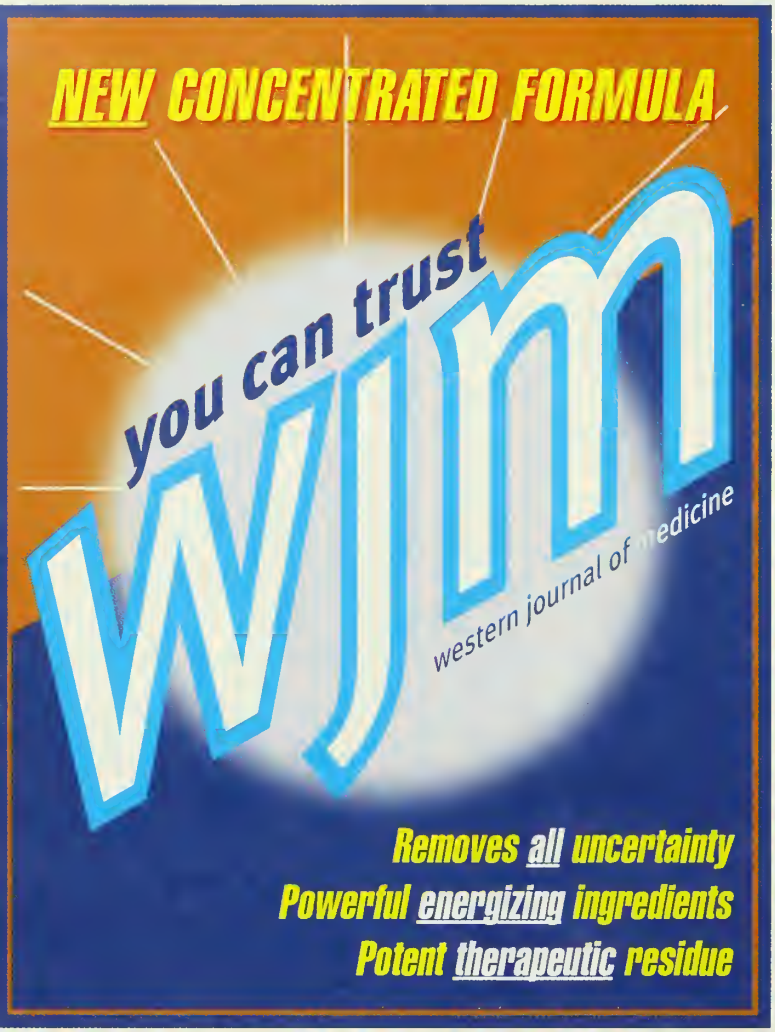
318 Guidelines for Authors

320 Visual Commentary
David Heiden

Op-Ed

To our readers

The new *WJM* will be informative, enjoyable and open to new ideas



This month's *Western Journal of Medicine* is the new *WJM*. From now on, the journal will be known by the abbreviation, *WJM*. The new *WJM* has a new look and novel content areas. The new design of the journal, and the increased attention to photography, art, medical graphics, and graphic design in our pages, will without a doubt make this a more visually appealing and exciting journal. We've also brought in new content by creating new sections, and by including medical writers who have not previously appeared in this journal. These changes are aimed at making *WJM* more intellectually stimulating, more clinically useful, and more enjoyable. Medicine Cabinet provides practical information on drugs, Evidence-Based Case Reviews offers well-referenced clinical guidance, Research Digest gives summaries of recent research, Med.Pix will be a regular feature on radiology, and our News section has in-depth reporting by journalists. Media Watch offers criticism of the media's coverage of medicine. Our section West of the Rockies introduces new columnists who will offer a regular perspective from the Southwest, the Northwest, and other regions.

We ask readers to submit clinical questions for the section Curbside Consult, and we will work hard to find the most qualified experts to respond. Of course, the new *WJM* will continue to include peer-reviewed, high-quality original research submissions, and we promise our authors a fast turnaround time in order to get new research information to our readers in a timely fashion. Stay tuned for further changes—an electronic version of the new *WJM* will be coming soon.

Michael S Wilkes, MD, PhD
mwilkes@ucla.edu

Miriam Shuchman, MD
shuchman@acsu.buffalo.edu

Rethinking case reports

Highlighting the extremely unusual can do more harm than good

Jerome R. Hoffman, MA, MD

Professor of Medicine
Emergency Medicine Center
924 Westwood Blvd
Los Angeles, CA
jrh@ucla.edu

In this month's transitional issue of the *WJM*, Wilkes et al. present the first in what we hope will be an innovative and informative series of case presentations, designed to bridge what is sometimes seen as a large gap between evidence based medicine (EBM) and clinical practice. It is important to contrast these presentations with traditional "case reports" found in many journals, as well as to address the role we hope they will play in helping transform the *WJM* into a reader-friendly yet erudite and sophisticated resource for clinicians in both community and academic practice.

Case reports are typically designed to highlight extremely unusual findings. Such reports generally take one of three forms: they describe a new or innovative treatment or approach to a particular disease, they address a rare condition, or they highlight very unusual manifestations of a common problem. Although each of these may be worth reporting, their utility for clinicians is likely to be extremely limited.

The first type of case report (describing a new approach or treatment) can raise a hypothesis that deserves further testing. Examples include the few case reports and small case series which suggested a possible role for high dose epinephrine in cardiac arrest, or those describing successful outcomes following serum alkalinization for tricyclic antidepressant poisoning. It would be foolhardy, however to translate the results derived in such noncontrolled "n of one" experiments to general clinical practice without much stronger evidence; indeed in many if not most such instances, the posited intervention has not proven useful when subjected to formal investigation.

Although the second type of case report (describing a rare condition) is also limited in utility, it remains useful because by definition there are not enough subjects who have any rare problem to allow it to be studied more rigorously. Nevertheless, by the same definition, few generalist clinicians will encounter such problems, and those who do are probably better served to consult textbooks for information about them. This is because by their nature these case reports do not present definitive evidence about the disease in question, and may focus on or stress elements that are misleading to physicians with extremely limited experience in dealing with the problem in question. While the opinions of experts (like those who are called upon to write book chapters) is subjective, it is undoubtedly helpful, in the absence of definitive evidence, to filter whatever information is available (including case reports) through their eyes.

The third type of case report, which describes a rare manifestation of a ubiquitous condition, is by far the most common, and unfortunately is far more likely to do harm than good. If an enterprising clinician tried to advance his or her career by writing up a case of an alcoholic patient whose gait was ataxic after a drinking binge, he or she would find it extremely difficult to find any journal willing to publish the case. Why? Because ataxia is an almost inevitable result of alcohol intoxication, and although it is a very useful finding, it is obviously familiar to most clinicians. If, on the other hand, the same author submitted a manuscript describing a patient who began to play the Bach Partitas and Sonatas, with perfect pitch and intonation, and great depth of feeling, immediately after an alcoholic binge (even though he had never before played the violin!), prestigious journals would surely vie for the opportunity to publish the case. Why? Because such a thing could never (or almost never) happen!

Indeed, a reasonable clinician, on reading the typical case report of this genre, would do well to take from it the exact opposite of whatever it purported to show. This is because the only reasonable interpretation of such a case is either a) the report is inaccurate (the patient was not drunk, or the beautiful music was actually coming from the CD player situated behind the drunk patient), or b) this was a miraculous event, destined to occur only once in a lifetime—and since it has already happened to the patient in the paper, it will almost certainly not happen again to your patients!

The literature-based case presentations that will appear in *WJM* are intended to be a very different animal. They will concentrate on common problems in primary care, regarding which the authors will be asked to address controversial issues, as well as approaches to diagnosis and treatment that can be supported by available evidence. They are not expected to be systematic reviews, that meet strict EBM standards for identifying and evaluating *all* available evidence. In general such formal reviews can only address limited or narrow questions, given the amount of work (and space) which must be expended on each separate question. Thus for a formal "systematic review" of congestive heart failure, the topic of our first case presentation, there would have to be extensive literature searches, and methodologic evaluations of all articles identified, for *many* separate subtopics, including the ability of different observers to interpret physical findings, the utility of various predictive instruments regarding prognosis, the efficacy of β-blockers and digoxin, the interaction between ACE-inhibitors and aspirin, etc. etc. Such an effort would be frankly prohibitive for our journal, nor do we imagine we could impose on many authors to try to tackle such an enormous task.

Nevertheless our case presentations, although not EBM reviews in a formal sense, remain very different from

both the classical case report model discussed above, and from many standard reviews where, with perhaps an occasional nod to the literature, so-called experts tell us what they do, and that we should do it too, because they're the experts! Written *by* practicing clinicians (with some help from experts, perhaps), and *for* practicing clinicians, these presentations are intended to be practical, down-to-earth, readable, and entirely supportable by the literature (rather than anecdotal experience). Thus they will be based on evidence, even if not formally "Evidence-Based."

WJM also expects to publish EBM-type systematic reviews, from time to time, of narrower clinical questions. These will serve a related, but slightly different, purpose. We believe there is room for both types of exercises, and that readers can benefit from each. Furthermore, we intend to carry a series of papers on the concepts, value, and limitations of EBM, which he hope will help elucidate these matters further. In the meantime, we hope that our case presentations, based on an honest attempt to find answers to clinically important questions about common problems faced in primary care, will be readable and interesting, and help readers improve clinical decision-making and optimize patient care. Happy reading!

Medical Futility

Physicians, not patients, call the shots

see also p.287

Charles Weijer, MD, PhD
Assistant Professor of Medicine
Bioethics Education and Research
Dalhousie University
5849 University Avenue, Room C-105
Halifax, Nova Scotia, CANADA, B3H 4H7
charles.weijer@dal.ca
Website: www.medicine.dal.ca/bioethics
Medical Research Council of Canada Scholar
Dalhousie University Clinical Scholar

The concept of medical futility, and the flurry of institutional policies spawned by it, embraces the normative illegitimacy described in *Through the Looking Glass*. When Alice challenges Humpty Dumpty for using words idiosyncratically, he responds: "'When I use a word,' Humpty Dumpty said, in a rather scornful tone, 'it means just what I choose it to mean—neither more nor less.' 'The question is,' said Alice, 'whether you can make words mean so many different things.' 'The question is,' said Humpty Dumpty, 'which is to be master—that's all.'"[1]

The term medical futility was coined in 1990 as a response to demands from patients and families for treatment thought by physicians to be inappropriate.[2] With the patients' rights movement cresting, it was widely believed that such demands would have to be acceded to unless new grounds for refusal were manufactured. Medical futility is designed, therefore, to be a trump card for physicians.

Futility is a professional judgment that takes precedence over patient autonomy and permits physicians to withhold or withdraw care deemed to be inappropriate without subjecting such a decision to patient approval.[2]

Futility is both unnecessary and philosophically unsound. Medical futility encompasses two kinds of cases. The first case involves treatment that is very unlikely to work. Physicians have never had an obligation to disclose or provide any conceivable treatment. With regard to disclosure of treatment options and the provision of medical interventions, physicians are held to the "standard of care," that is, the range of treatment accepted by at least a minority of expert practitioners. If a treatment is widely accepted as ineffective, it follows that the physician—without need of appeal to the notion of medical futility—has no obligation to disclose or provide such treatment.[3]

Futility's harm comes from its inclusion of a second kind of case.[4] In it the treatment is effective, but the end supported, for example, maintaining a patient in persistent vegetative state, is controversial. Often the question, "What sort of life is worth preserving?" is at the heart of these disputes. Not surprisingly, many of best known cases in the literature involve families who demand continued treatment on the basis of strongly held cultural or religious beliefs.[5] Futility does harm by suggesting that physicians should, "Just say no." Rather, good medicine requires that doctors practice with respect for such beliefs and, therefore, open communication and negotiation is the morally preferred course of action.

One wouldn't guess it from the size of the medical literature on medical futility—445 articles as of January 1999—but disagreements with regard to the provision of life-prolonging care are uncommon. Patients and families disagree with recommendations to limit life-sustaining care infrequently, and these disagreements tend to resolve in a few days.[6] Given this, one has to wonder, "What else is driving the agenda?" Prolonged disputes often involve a substantial disagreement in values between the patient and the physician.

Futility's response to the question, "Which is to be master?" is clear: the values of the physician. Seen this way, futility, and policies based upon it, attempts to exchange shared decisionmaking for medical paternalism; in short, it is an attempt to undo the bulk of moral progress made in medicine over the last thirty years.

References
1. Carroll L. *Alice's Adventures in Wonderland and Through the Looking-Glass*. New York: Oxford University Press, 1982:190.
2. Schneiderman LJ, Jecker NS, Jonsen AR. Medical futility: its meaning and ethical implications. *Ann Intern Med* 1990; 112:949-954.
3. Weijer C, Singer PA, Dickens BM, Workman S. Bioethics for clinicians: 16. Dealing with demands for inappropriate treatment. *Can Med Assoc J* 1998 159: 817-821.
4. Weijer C, Elliott C. Pulling the plug on futility. *Br Med J* 1995; 310: 683-684.
5. Weijer C. Cardiopulmonary resuscitation for patients in persistent vegetative state: futile or acceptable? *Can Med Assoc J* 1998; 158: 491-493.
6. Smedira NG, Evans BH, Grais LS, Cohen NH, Lo B, Cooke M, et al. Withholding and withdrawal of life support from the critically ill. *N Engl J Med* 1990; 322:309-315.

Mail

The power of herbs • A warm welcome

The Power of Herbs

To the Editors,

Five years ago my neighborhood supermarket had a single shelf of vitamins. Now almost an entire aisle is taken up with hundreds of "natural health" preparations. The greatly expanded offering of vitamins has been joined by an alphabetized bank of herbal capsules, a wall of herbal teas, and an impressive *materia medica* of homeopathic remedies. Various formulations of St. John's Wort alone command as much space as the vitamin shelf of a half decade ago. The supermarket doesn't stock these items out of idealism. It stocks them because they sell. The same shopper who hesitates to use a prescribed decongestant will grab a bottle of *ephedra* capsules on the way to the check-out stand. Never mind that the herbal preparation might have the exact same active pharmacologic agent as the decongestant—but in a haphazard, uncontrolled mixture that has almost certainly never undergone tests for efficacy and potential side-effects. If it looks like powdered green weed in a capsule, it must somehow be better for you than an artificially colored pill.

"Why don't you try this?" my cousin said, holding up a small brown bottle with a plain typewriter label. "It is dog fat—rendered oil from a dog. The herbalist in the village recommends it for colds."

Eighty years after the Flexner report tried to do away with unscientific medicine, the pillars of the American medical community have called a truce in their battle with the holistic health care practitioners. They have bowed to market forces. The reality today: herbs are big. We now have an Office of Alternative Medicine, which some politicians are pushing to be elevated to a full member of the National Institutes of Health. Medical schools are adding courses in "complementary medicine" that are enormously popular. And even the hesitantly conservative *Medical Letter* has given the nod to some herbal remedies, reviewing them along with their pharmaceutical counterparts. In some states, naturopathic physicians are demanding admission privileges to hospitals.

I look on all this with bemusement, and listen politely when my patients ask me whether they should take erythromycin or *echinacea* for a culture-positive strep throat. After all, I have been experimenting eagerly with herbs for twenty years—long before the current popularity, and before most of the public had even heard of these remedies. Whenever I travel, in Africa, Asia, or Central America, I like to check out the corner apothecary or the market herbalist to see what exotic nostrums are used for various ailments. And whenever the opportunity has arisen, I like to try some of these remedies myself. I've submitted to a shamanic ritual for a shoulder injury in Kenya, drunk foul potions for recurrent bronchitis in Nepal, and almost choked on some dust-like herb for what was probably an acute staphylococcal gastroenteritis in Taiwan. Did the remedies work? The shoulder did, in fact, eventually get better, after about a year. Getting out of the smoky huts in Nepal probably assisted whatever curative powers the herb supplied. And I must say, my vomiting and diarrhea were relieved not long after I gagged down the dusty mixture. Perhaps I would be unfair to suggest that most acute gastroenteritis resolves spontaneously anyway.

Six years ago I found myself with a nasty cold while visiting a cousin in Switzerland. My cousin is a farmer in the Appenzell—a region analogous to rural Appalachia in the United States with a quirky folk culture that makes it the butt of a lot of national jokes. At the time of my visit, I had been working at a busy family

Advice to authors

We prefer to receive all responses electronically as e-mail or on a disk. Processing your letter will be delayed unless it arrives in an electronic form. Responses should be under 400 words and relate to articles published in the preceding three months. They should include <5 references, in the Vancouver style, including one to the *WJM* article to which they relate. We welcome illustrations. Please supply each author's current appointment and full address, and phone, fax or e-mail details for the corresponding author. We ask authors to declare any competing interest. Letters will be edited and may be shortened.

wjmsf@pacbell.net

practice and was coming down with three or four viral upper respiratory infections myself every year, the inevitable consequence of bad food, not enough sleep, and treating countless sneezing and sniffling patients. I was not enthusiastic about enduring these same symptoms during my short vacation in Switzerland.

"Why don't you try this?" my cousin said, holding up a small brown bottle with a plain typewriter label. "It is dog fat—rendered oil from a dog. The herbalist in the village recommends it for colds."

I pried off the cap, took a whiff, and poured a slight amount onto my fingers. It had a greasy feel and distinct odor of wet dog.

"I recommend you take it with some brandy—might make it a bit easier to go down," he added helpfully when he saw the look of distaste on my face.

"Does it work?" I asked.

> "It occurred to me that my cold was just about gone anyway."

"Well," he admitted sheepishly, "I've never actually tried it. Take it. You can have the bottle." I looked at him skeptically. He quickly added, by way of explanation, "You know, I never get sick, so I don't really need it."

I studied the brown bottle. The label advised a teaspoon, preferably warm, three times a day between meals, and pleasantly suggested that the elixir might be combined with fresh lemon juice and honey. It occurred to me that my cold was just about gone anyway.

Trying the dog fat now wouldn't really be a fair trial, would it? Better to wait until the next cold. Yes, I would keep this bottle and right at the prodrome, I would take it according to the directions.

For the past six years the bottle has sat in my bathroom cabinet, right next to the ibuprofen, the cologne, and the skin moisturizer.

Whenever I feel the first hint of a cold—a vague feverish discomfort, slightly burning face, or irritable sore throat—I look at that brown flask. Hundefett. It is still completely full, since my symptoms somehow vanish and I have never again come down with a cold.

Paul Gahlinger, MD, PhD, MPH
88 K Street
Salt Lake City, UT 84103

A Warm Welcome

Dear Drs Wilkes and Shuchman,

A warm welcome to the all-new *WJM!* We are excited about the changes to the journal. We feel that the new journal will offer our physicians practical clinical information of the highest quality. You and your editorial board worked hard on this relaunch, and your efforts are reflected in the many new sections, such as Best Practice and Culture and Medicine, intended to create an enjoyable, readable, and trustworthy journal. We also eagerly await eWJM, the user-friendly, web-based collection of articles, reviews, pictorial quizzes, and medical events occurring in the Western states and provinces.

Most importantly, we look forward to working with you to assure that health care practitioners receive the type of clinical information they need to continue improving patient care as we head into the new millennium. We hope these new ideas will both stimulate and remind them of the glories of practicing medicine even in this difficult environment.

We welcome *WJM* and wish you the very best!

Jack Lewin, MD
EVP/CEO, California Medical Association

George P Bunch, MD
President, New Mexico Medical Society

Robert K Seehusen
Executive Director and CEO, Idaho Medical Association

Original Research

Analysis of Chinese herbal creams prescribed for dermatological conditions

F M Keane
S E Munn
A W P du Vivier
E M Higgins

Department of Dermatology
King's College Hospital,
London SE5 9RS

N F Taylor

Department of Clinical Biochemistry
King's College Hospital,
London SE5 9RS

Correspondence to:
Dr Keane,
FionaKeane99@hotmail.com

Funding: None.
Competing interests: None declared.

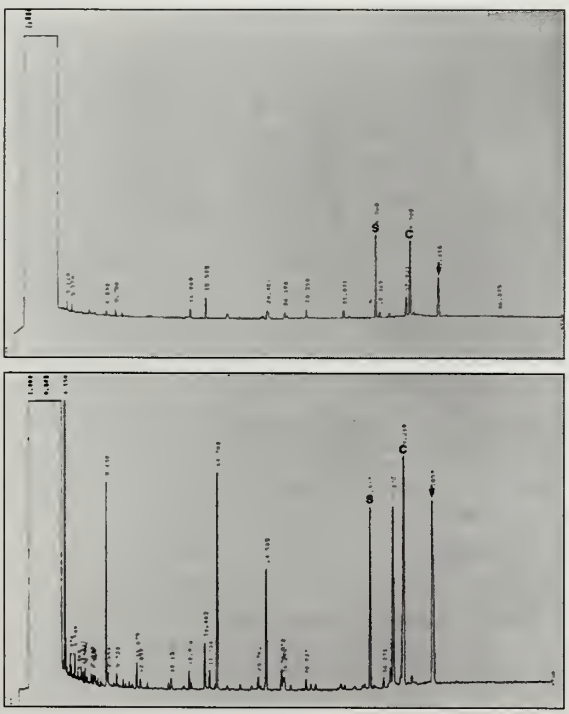
ABSTRACT ● **Objective** To determine whether Chinese herbal creams used for the treatment of dermatological conditions contain steroids. ● **Design** 11 herbal creams obtained from patients attending general and pediatric dermatology outpatient clinics were analyzed with high resolution gas chromatography and mass spectrometry. ● **Setting** Departments of dermatology and clinical biochemistry. ● **Main outcome measure** Presence of steroid. ● **Results** Eight creams contained dexamethasone at a mean concentration of 456 μg/g (range 64 to 1500 μg/g). All were applied to areas of sensitive skin such as face and flexures. ● **Conclusion** Greater regulation needs to be imposed on Chinese herbalists to prevent illegal and inappropriate prescribing of potent steroids.

Introduction

Alternative therapies are becoming increasingly popular, particularly among patients with chronic skin disorders such as eczema, which are not cured by standard treatment. Parents of children with eczema and adult patients tend to regard herbal remedies as natural, plant-derived products that are without side effects. In particular, they believe them to be free of steroids, unlike many of the treatments prescribed by primary care physicians or dermatologists. Oral Chinese herbal preparations have been the subject of discussion for some time and have been shown to be of benefit in eczema.[1, 2] In practice, however, Chinese herbalists often prescribe creams, either alone or in conjunction with the oral preparations.

We became interested in Chinese herbal medicine because several of our patients reported improvement of their eczema when using alternative treatments. Many returned to our clinic when they could no longer afford the herbs (the cost was up to $56 per week) with either an exacerbation of their eczema during herbal treatment or a request to continue their treatment through the National Health Service. We suspected that these herbal creams contained a steroid, so we analyzed some of them.

Figure 1 Gas chromatograms of standard cream containing dexamethasone *(top)* and Chinese herbal cream *(bottom)*.



S=peak for internal standard 1, C=peak for internal standard 2, ↓=peak for dexamethasone

Methods

Ten patients submitted Chinese herbal creams for analysis (seven children, three adults). One adult was using two creams, giving a total of 11 for analysis. Four patients were simultaneously taking oral preparations. Their ages ranged from 4 months to 36 years. Five different suppliers in south London were identified.

The cream was weighed and then mixed with ethyl acetate and water using a vortex. The phases were separated by centrifugation, and the organic phase was filtered through phase separating paper. This was evaporated, usually leaving an oily residue which solidified on cooling.

The oil in the residue was removed by liquid-gel chromatography. A portion of the purified extract was analyzed as a derivative on a gas chromatograph. Peaks were compared with known standard steroid peaks (Figure 1). The identity of peaks was confirmed by mass spectrometry of standard dexamethasone and selected test creams.

Results

Ten of the 11 creams were white with an aromatic smell. Most containers were small glass pots, which were either unlabeled or labeled only with the name of the cream or

Table 1 *Dexamethasone content of Chinese herbal medicines prescribed for skin disorders and perceived effect*

Name of cream	Dexamethasone (μg/g)	Clinical indication	Clinical effect
Skinpro skin care lotion	0	Eczema herpeticum	Exacerbation
Unlabeled	60	Eczema herpeticum	Exacerbation
Unlabeled	84	Eczema	Improvement
Pyong ping	740	Eczema	Improvement
Yellow lily paste	0	Scaly scalp	No benefit
Skin care No 1	227	Eczema	Improvement
Skin care No 1	334	Eczema	Improvement
Skin care No 1	460	Eczema	Improvement
Unlabeled	0	Scaly scalp	No benefit
Ointment to ease inflamed skin	1512	Eczema	Improvement
Unlabeled	640	Eczema	Improvement

supplier and frequency with which to apply the cream. Two pots were labeled with Chinese writing indicating the ingredients of the cream which included yellow lily, *Radix astragali, Herba menthae,* and *Radix angelica pubescentis.* The indications for prescribing the treatment were eczema in seven cases, scaly scalp in two, and eczema herpeticum in one case (Table 1).

Eight of the 11 creams contained dexamethasone at a mean concentration of 456 μg/g (range 64 to 1500 μg/g). The two bottles labeled with the ingredients did not contain dexamethasone. All the creams prescribed for eczema (including one case of eczema herpeticum) contained dexamethasone. The concentration of dexamethasone in creams prescribed for children was 5.2 times higher than that in those prescribed for adults (654.6 μg/g v 125 μg/g respectively). The highest concentration was prescribed for the face of a 4-month-old baby with eczema.

All of our patients were unaware of the ingredients of the creams but had assumed that they did not contain steroids. As none had been given advice about potential side effects, the creams had been applied to the face and the flexures, often several times a day.

Discussion

Dexamethasone is a potent steroid. The mean dose of 456 μg dexamethasone/g cream is roughly equivalent to 0.05% betamethasone valerate, which is a more familiar preparation in the United Kingdom. The risk of side effects with such potent steroids is increased by their inappropriate use and application to areas of thin skin such as flexures and the face. We do not know the original source of the preparations or whether they all came from the same supplier. The varying amounts of steroid found in each cream, however, suggest that some preparation and mixing occurred at each shop.

Chinese herbal medicines are widely available. Concern about the arbitrary supply of herbs for oral use, the dose and content of which are apparently individually tailored, has already been voiced by dermatologists and hepatologists.[3, 4] The source and quality of the ingredients is also not standardized. Hepatotoxicity has been reported from oral preparations, and little is known about the long term toxicity of these drugs. Sheehan et al have shown that standardized oral herbal preparations that are monitored in a conventional Western manner are beneficial in eczema.[1, 2] They also reported that these standardized preparations did not act like steroids. In our experience, however, most patients receive "personalized," unlabeled, and unstandardized preparations.

In 1990, it was suggested that the improvement noted during treatment with oral herbs might be due to a steroid in the cream that was concurrently prescribed. This theory, however, was never substantiated.[5] Subsequently, the illegal supply of labeled oral[6] and topical[7] steroids by Chinese herbalists has been reported. Our patients received both unlabeled and unlicensed topical treatment. Our results indicate that in many instances when patients receive combination oral and topical treatment, the topical element (which is essentially an unlicensed steroid) contributes to the clinical response. What must also be considered is the ethical issue arising from giving steroids to patients who, disillusioned with conventional treatment, believe they are taking herbal preparations that do not contain steroids.

Chinese herbal creams are marketed, admittedly by word of mouth, as safe and steroid free. Although our sample numbers were small, most creams that we tested, including all of those prescribed for eczema, contained steroids.

We thank Elizabeth VEM Okokon for help with the steroid analysis.

Contributors: FMK designed the project, collated the data, and wrote the paper. SEM helped in the design of the project and collection of creams for analysis. NFT analyzed the steroids. EMH and AWPduV coordinated the research and are guarantors for the paper.

This paper was originally published in the *BMJ* 1999; 318:563-4.

References
1. Sheehan MP, Rustin MHA, Atherton DJ, Buckley C, Harris DJ, Brostoff J, et al. Efficacy of traditional Chinese herbal therapy in adult atopic dermatitis. *Lancet* 1992; 340:13-7.
2. Sheehan MP, Atherton DJ. A controlled trial of traditional Chinese medicinal plants in widespread non-exudative atopic eczema. *Br J Dermatol* 1992; 126:179-84.
3. MacGregor FB, Abermethy VE, Dahabra S, Cobden I, Hayes PC. Chinese herbs for eczema. *Lancet* 1989; 299:1156-7.
4. Kane JA, Kane SP, Jain S. Hepatitis induced by traditional Chinese herbs; possible toxic components. *Gut* 1995; 36:146-7.
5. Allen BR, Parkinson R. Chinese herbs for eczema. *Lancet* 1990; 336:177.
6. O'Driscoll J, Burden AD, Kingston TP. Potent topical steroid obtained from a Chinese herbalist. *Br J Dermatol* 1992; 127:543-4.
7. Hughes JR, Higgins EM, Pembroke AC. Dexamethasone masquerading as a Chinese herbal. *Br J Dermatol* 1994; 130:261.

Summary Points

- Patients with eczema often report improvement with Chinese herbal creams
- There may be no indication on the label about the contents of the cream
- Eight of the 11 creams analyzed contained dexamethasone at concentrations inappropriate for use on the face or in children
- Inadvertent use of topical steroids can cause severe exacerbation of eczema herpeticum
- Closer regulation of herbal medicines is required

COMMENTARY
Adulterants in herbal products: dangerous and deceitful

Stephen Bent

Osher Center for Integrative Medicine, University of California, San Francisco, San Francisco Veterans Affairs Medical Center, San Francisco, CA
bent@itsa.west.edu

The herbal product industry in the United States is booming. Annual retail sales are approaching $4 billion and growing about 18% per year.[1] Botanicals are appearing not only in a multitude of over-the-counter pills and extracts, but also in a variety of food products including teas, soft drinks, soups, and even potato chips. Up to a third of American adults are now routinely using herbs to enhance health or alleviate illness.[1]

Because herbal products come from plants, they are often viewed as "natural" and free from serious side effects. Unfortunately, herbs are not inherently safe. Recent reports have highlighted severe reactions both to specific herbs, and to contaminants in the preparations.[2,3] Reactions range from mild side effects such as transient hepatitis or dermatitis, to severe fatal illnesses including anaphylactic shock and liver failure.[2] A recent study of 260 traditional Chinese medicine products sold in California retail herb stores found that 32% contained undeclared pharmaceuticals or heavy metals.[4] Contaminants found in herbal preparations include lead, mercury, arsenic, diazepam, thiazide diuretics, ephedrine, and caffeine. The true incidence of side effects to herbal products is not known because the systems for reporting adverse reactions are limited.

How can the consumer be sure that an herbal product is both safe and effective? In the United States, most herbs are sold as dietary supplements, and are therefore regulated by the Dietary Supplement Health and Education Act (DSHEA) of 1994. Under this legislation, herbs and other dietary supplements (including vitamins, minerals, plant-derived substances, and amino acids) may be sold and marketed without approval by the Food and Drug Administration (FDA).[5] The DSHEA specifies that the manufacturer is responsible for ensuring the safety of the herbal product. However, there is no standard describing the specific tests required to document safety, and therefore manufacturers may vary widely in the amount of testing performed. This system is in sharp contrast to that in place for standard drugs, where the manufacturer must submit adequate evidence of safety and efficacy to the FDA before the product may be sold.

The labeling of herbal products sold as supplements is even more confusing. Supplement labels may not make statements that imply that the product helps to diagnose, treat, cure, or prevent a disease. Supplements may, however, make certain "structure-function" claims. For example, a product may claim to "maintain bowel regularity" or "support immune function," but it cannot claim to "relieve constipation" or "treat the common cold." If supplements were used for these specific purposes, they would be considered drugs, and would be subject to a much more stringent regulatory process.

In this issue of *WJM,* Keane et al report a disturbing finding about the contents of a sample of Chinese herbal creams that highlights some of the problems with the regulation of the herbal products.[6]

Intentionally adding active ingredients to herbal preparations without the knowledge of patients is illegal, dangerous, and deceitful. In the United States, any agent that is used to treat a specific condition (such as eczema) is considered a drug, and must undergo approval by the FDA prior to marketing and distribution. In this study, the dose of steroids used would have required a prescription, which is yet another level of wrongdoing. Clearly this dose of steroid can be dangerous for patients, especially if used on the face or in children, as was the case in this report. And perhaps most worrisome, the practice of treating patients without telling them the active ingredients of the treatment and the associated risks and benefits is deceitful.

Chinese herbal treatments (without steroids) may indeed be effective for the treatment of eczema, as suggested

by earlier reports.[7,8] Although these studies are preliminary and not conclusive, they deserve further investigation. In general, the use of herbs in traditional Chinese medicine involves an examination by a Chinese doctor, an assessment of the patient's disorder, and the prescription of an individualized herbal treatment. While this practice is foreign to our westernized vision of medicine, it may have unique merits, and there is evidence to suggest that certain Chinese herbal remedies are effective.[7-9] Given the high prevalence of use and the potential benefit of these therapies, we must investigate their effectiveness with an open mind and with a rigorous scientific method. We must also support government efforts to locate practitioners that are exposing patients to illegal and dangerous treatments, thereby tarnishing the name of traditional Chinese medicine.

References

1. Brody JE. Americans gamble on herbs as medicines. *New York Times.* February 9, 1999:D1.
2. Ernst E. Harmless herbs? A review of the recent literature. *Am J Med.* 1998; 104:170-178.
3. Slifman NR, Obermeyer WR, Aloi BK, et al. Contamination of botanical dietary supplements by Digitalis Lanata. *NEJM.* 1998; 339:806-811.
4. Ko RJ. Adulterants in Asian patent medicines. *NEJM.* 1998; 339:847.
5. Mitka M. FDA never promised an herb garden—but sellers and buyers eager to see one grow. *JAMA.* 1998; 280:1554-1556.
6. Keane FM, Munn SE, du Vivier AWP, Taylor NF, Higgins EM. Analysis of Chinese herbal creams prescribed for dermatological conditions. *West J Med.* 1999:
7. Sheehan MP, Rustin MHA, Atherton DJ, et al. Efficacy of traditional Chinese herbal therapy in adult atopic dermatitis. *Lancet.* 1992; 340:13-17.
8. Sheehan MP, Atherton DJ. A controlled trial of traditional Chinese medicinal plants in widespread non-exudative atopic eczema. *Br J Dermatol.* 1992; 126:179-184.
9. Bensoussan A, Talley NJ, Hing M, Menzies R, Guo A, Meng N. Treatment of irritable bowel syndrome with Chinese herbal medicine. *JAMA.* 1998; 280:1585-1589.

Historical cohort study of in utero exposure to uterotonic drugs and cognitive function in young adult life

ABSTRACT ● **Objective** To examine whether in utero exposure to uterotonic drugs effects cognitive performance in draft-age men. ● **Design** Historical cohort study based on birth registry data and cognitive function measured during evaluations for military service. ● **Subjects** 4300 Danish conscripts born between 1973 and 1975. ● **Main outcome measures** Mean score in the Boerge Prien test of cognitive function: score is the number of correct answers to 78 questions and correlates with the full scale intelligence quotient. ● **Results** The mean Boerge Prien score was similar for those exposed (n=1011) to uterotonic drugs and those not exposed (n=3289), 43.1 versus 42.9 after adjustment for confounders. ● **Conclusion** Our data indicate that exposure to uterotonic drugs does not affect cognitive function 20 years later.

Henrik Toft Sørensen
Department of Internal Medicine V, Aarhus University Hospital, 8000 Aarhus C, Denmark

Flemming Hald Steffensen

Svend Sabroe
Danish Epidemiology Science Center, Department of Epidemiology and Social Medicine, University of Aarhus, 8000 Aarhus C

Kenneth J Rothman
Department of Epidemiology and Preventive Medicine, Boston University School of Medicine, Boston, MA 02118

Matthew W Gillman
Department of Ambulatory Care and Prevention, Harvard Medical School and Harvard Pilgrim Health Care, Boston, MA 02215

Peer Fischer
Conscription Administration, County of North Jutland, 9000 Aalborg, Denmark

Correspondence to:
Dr Sørensen
hts@soci.au.dk

Conflict of interest: None declared.

Oxytocin has potent uterotonic properties that can induce tetany, rupture, and water intoxication. Inappropriately high doses can affect the fetus by inducing abnormal heart rhythms, circulatory collapse, and preterm delivery accompanied by an increased risk of respiratory distress and damage to the central nervous system.[1] Several studies have reported an association between oxytocic drugs and neonatal hyperbilirubinemia,[2] which might influence long-term cognitive function.[3] Little is known, however, of the long term consequences of exposure to uterotonic drugs. We investigated whether in utero exposure to uterotonic drugs affects cognitive performance in men of draft age.

Subjects, methods, and results

Nearly all Danish men have to register with the draft board at around 18 years of age, at which time they undergo physical and mental examinations. We studied all men who were born in Denmark after January 1, 1973 and who were drafted while residing in North Jutland and Viborg counties from August 1, 1993 to July 31, 1994.

All draftees took a 45-minute intelligence test, the Boerge Prien test, developed in 1957 for the Danish draft board.[4] The test includes four time-limited subtests covering four categories: letter matrices, verbal analogies, number series, and geometric figures. The test shows high correlations with the Weschler Adult Intelligence Scale verbal intelligence quotient (0.78), the performance intelligence quotient (0.71), and the full scale intelligence quotient (0.82). In the validation study the mean full scale intelligence quotient was 106, equivalent to a mean Boerge Prien test score of 44.2.[4]

We linked data from the draft examination with data from the Danish medical birth registry using a 10-digit unique personal identification number. The registry contains information on all births in Denmark since 1973. Oxytocin was the most commonly used uterotonic drug in

Table 1 *Data on 4300 Danish draftees according to exposure to uterotonic drugs during delivery. Figures are numbers (percentages) of subjects unless stated otherwise**

		Not exposed (n=3289)	Exposed (n=1011)
Draftees	Boerge Prien test score:		
	Median (range)	44 (5-69)	44 (9-68)
	Mean (95% CI)	43.1 (42.8 to 43.4)	42.9 (42.3 to 43.5)
	Quartiles (1-3)	37-50	37-49
	Median (range) birth weight (g)	3380 (1130-5380)	3630 (1630-5380)
	Quartiles of birth weight (1-3)	3130-3800	3130-3880
	Median (range) birth length (cm)	52 (39-62)	53 (40-61)
	Quartiles of birth length (1-3)	51-54	51-54
	Gestational age (weeks):		
	≥ 37	2974 (90.5)	926 (91.6)
	34-36	222 (6.8)	62 (6.1)
	≤ 33	92 (2.8)	23 (2.3)
	Number delivered by Caesarean section	188 (5.7)	76 (7.5)
Mothers	Median (range) age (years) at delivery	26 (15-43)	26 (16-43)
	Quartiles of age (1-3) at delivery	23-29	23-29
	Parity:		
	0-1	2261 (68.7)	724 (71.6)
	2	638 (19.4)	172 (17.0)
	≥3	390 (11.9)	115 (11.4)
	Employment 3		
	Unemployed, housewife, retired	869 (26.6)	222 (22.1)
	Employed	2219 (67.9)	737 (73.5)
	Self-employed, assisting spouse	179 (5.5)	44 (4.4)

*Total number of subjects is not always 4300 because some data were missing.

that period. We examined the mean Boerge Prien test score according to in utero exposure to uterotonic drugs, taking account of possible confounding variables (Table 1).

We identified 4805 conscripts during the study period. We had complete draft medical data on 4300. Of the remainder, 495 were exempt from the examination mainly because of asthma, osteochondrosis, and epilepsy, and 10 had incomplete data in the birth registry. Of the 4300 with complete medical data, 22.8% had been exposed to uterotonic drugs; among those who were exempt from the examination, 23.5% had been exposed to uterotonic drugs.

The mean Boerge Prien score was similar for those exposed and those not exposed to uterotonic drugs (43.1 v 42.9). We also stratified the subjects by mode of delivery; in subjects born by vaginal delivery the mean Boerge Prien score was 43.0 among those exposed to uterotonic drugs compared with 43.1 among those not exposed. From a multiple linear regression with all above mentioned confounding variables included we estimated the difference in Boerge Prien score to be −0.58 (95% confidence interval −1.25 to 0.08) between those exposed and those not exposed to uterotonic drugs.

Comment

Friedman et al examined 156 children from 23 to 62 months after births associated with spontaneous labor, labor induced with oxytocin, or labor induced with dinoprostone. The overall prevalence of neurological or developmental abnormalities not attributable to events after delivery was the same in induced and spontaneous labors, but those abnormalities occurring after the induction of labor all followed the use of oxytocin.[5] Our data indicate that exposure to uterotonic drugs does not substantially affect cognitive function 20 years later. A small difference due to nondifferential misclassification, however, cannot be ruled out. A strength of our study is the large size, the population-based design, and complete ascertainment. It is unlikely that selection bias and confounding explain the lack of association.

Contributors: HTS, KJR, and MWG in collaboration with SS initiated the establishment and design of the cohort. HTS initiated this study and discussed the hypothesis with KJR. HTS and FHS analysed the data. PF collected the outcome data. SS linked the data to the birth registry. All authors participated in the interpretation of the findings. HTS, KJR and FHS wrote the first draft of the paper. All participated in editing the paper. HTS is guarantor of the paper.

Funding: Helsefonden (grant number 11/064-94), the EU Biomed II programme (contract number BMH4-CT97-2430), Aarhus University Research Foundation (F-1996-SUN-1-77), and the Danish Medical Research Council (grant No 9700677). The activities of the Danish Epidemiology Science Center are financed by a grant from the Danish National Research Foundation.

This paper was originally published in the *BMJ* 1999; 318:433-4.

References
1. Dawood MY. Evolving concepts of oxytocin for induction of labor. *Am J Perinatal* 1989; 6:167-72.
2. Johnson JD, Aldrich M, Angelus P, Stevenson DK, Smith DW, Herschel MJ, et al. Oxytocin and neonatal hyperbilirubinemia. *Am J Dis Child* 1984; 138:1047-50.
3. Seidman DS, Paz I, Stevenson DK. Neonatal hyperbilirubinemia and physical and cognitive performance at 17 years at age. *Pediatrics* 1991; 88:828-33.
4. Mortensen EL, Reinisch JM, Teasdale TW. Intelligence measured by WAIS and a military draft board group test. *Scand J Psychol* 1989; 30:3115-18.
5. Friedman EA, Sachtleben MR, Wallace AK. Infant outcome following labor induction. *Am J Obstet Gynecol* 1979; 133:718-22.

COMMENTARY

Long-term cognitive effects of drugs used during labor

Kristine Yaffe

Department of Psychiatry and Neurology, University of California, San Francisco, 4150 Clement Street, San Francisco, CA 94121

Sumner J Yaffe

Center for Research on Mothers and Children, National Institute of Child Health and Human Development, National Institutes of Health, Building 61, Bethesda, MD 20892

Oxytocin, a hormone produced by the posterior pituitary gland, stimulates uterine smooth muscle during labor, contracts uterine vessels, and induces milk letdown. It is available as a synthetic compound and is used to induce uterine contraction during labor in 15-40% of parturients and to diminish blood loss in almost all women during the final stage of labor.[1] High doses of oxytocin may result in hyperstimulation of the uterus and may pose an appreciable risk to the mother and fetus; risks to the fetus include hypoxia and damage to the central nervous system.[2] The long-term consequences for the infant of oxytocin and other commonly used drugs have not been well studied. In particular, the behavioral and cognitive outcomes of pharmacological treatments used during labor have received little attention. This has partially been due to the tremendous expense of and difficulty in following cohorts of infants and studying them over decades.[3] The challenge of adjusting for potential confounders (such as socioeconomic, nutritional and educational status) from the time of exposure in utero through to adulthood are also enormous.

Sorensen et al have met some of these challenges with their study of a cohort of 4300 draft-age men from two Danish counties who completed a Danish intelligence test, the Boerge Prien test, as part of the screening examination for the draft.[4] The draftees were linked to the Danish medical birth registry, a database containing data on all births since 1973. Altogether, 1011 (22.8%) of the men had been exposed to oxytocin in utero; their mean intelligence score was not significantly different from those who were not exposed, even after multivariate adjustments. This rare opportunity to follow a cohort from birth to adulthood with complete ascertainment is laudable. Further strengths of the study are its large sample size and its community-based population.

More information on the dose of oxytocin and, most importantly, at which stage of labor it was administered would have provided more conclusive evidence. Exposure during the third stage of labor (postpartum) would not be expected to affect the newborn whereas exposure during earlier stages might have an effect on the central nervous system of the fetus.[5] In addition, a selection bias could explain the lack of an association since 495 men were exempted from the examination on medical grounds due to illnesses which included epilepsy. Although the percentage of those exposed to oxytocin was similar for the men who were examined and those who were not, it would have been useful to determine if those with epilepsy had had a similar exposure rate. Epilepsy is often an indication of widespread central nervous system injury[6] that, in turn, may be associated with poor cognitive function. It would also have been useful to determine the educational performance of the cohort to see if functional differences existed between the exposed and unexposed groups. It is also possible that gender differences exist; Seidman et al found that neonatal hyperbilirubinemia was associated with lower scores on intelligence tests in male 17-year-olds but not in females.[7] Interestingly, they did not find a significant association between IQ score and hyperbilirubinemia when it was analyzed as a continuous variable but did when IQ was dichotomized to a low score. It would be interesting to explore whether Sorensen et al stratified the groups by performance and if there was an association between poor performance and exposure to oxytocin.

Long-term consequences, especially cognitive and behavioral, of drugs administered during labor and delivery have not been studied often. The findings by Sorensen et al are a significant contribution towards answering an important question. More research on the effects of drug exposure in utero should be pursued.

References
1. Carey J, Katz C. Drugs used in labor and delivery. In: Yaffe SJ, Aranda JV, eds. *Pediatric pharmacology.* 2nd ed. Philadelphia: WB Saunders, 1992:128-142.
2. Physicians' desk reference. 52nd ed. Montvale, NJ: Medical Economics Company, 1998.
3. Klebanoff MA, Zemel BS, Buka S, Zierler S. Long-term follow-up of participants in the collaborative perinatal project: tracking the next generation. *Paediatr Perinat Epidemiol* 1998; 12:334-46.
4. Sorensen HT, Rothman KJ, Gillman MW, Steffensen FH, Fischer P, Sabroe S. Historical cohort study of in utero exposure to uterotonic drugs and cognitive function in young adult life. *BMJ* 1999; 318:433-4.
5. Prendiville W, Elbourne D, Chalmers I. The effects of routine oxytocic administration in the management of the third stage of labour: an overview of the evidence from controlled trials. *Br J Obstet Gynaecol* 1988; 95:3-16.
6. Nelson KB, Ellenberg JH. Predisposing and causative factors in childhood epilepsy. *Epilepsia* 1987; 28(suppl 1):16-24S.
7. Seidman DS, Paz I, Stevenson DK, Laor A, Danon YL, Gale R. Neonatal hyperbilirubinemia and physical and cognitive performance at 17 years of age. *Pediatrics* 1991; 88:828-33.

Med.Pix

HERPES ZOSTER DISTRIBUTION—A LESSON IN ANATOMY

Is herpes zoster unilateral?

QUESTION: The Varicella zoster virus (VZV) follows a dermatomal distribution and unless disseminated, the reactivation of this virus is thought to be unilateral. Why do the lesions in Figures 1 and 2 appear to cross the midline?

Richard P Usatine

Carmine Clemente

University of California
Los Angeles, CA

Correspondence to:

Dr R Usatine
rusatine@ucla.edu

Figure 1

Figure 2

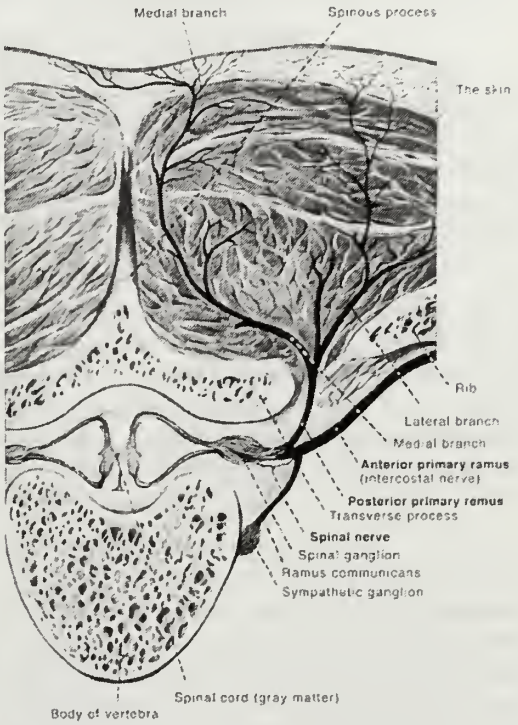


Figure 3

ANSWER: The answer lies in the anatomy of the spinal nerves (Figure 3). The posterior primary ramus of each spinal nerve has a small medial branch and a larger lateral branch. Therefore, the cutaneous innervation to the back is crossed with the medial branch, only reaching a few centimeters across the midline.

These clinical photographs of two different cases of zoster demonstrate the anatomy of the spinal nerves. These cases are not disseminated zoster, but each case represents a single dermatome innervated by a single spinal nerve showing cross-innervation. Both cases were in otherwise healthy young adults. Neither patient developed disseminated zoster nor was found subsequently to have any underlying illness.

Most zoster cases are acutely painful, uncomplicated, and resolve spontaneously in 1 to 2 weeks. Disseminated zoster can occur in immunosuppressed individuals. The VZV remains latent in the dorsal root ganglia and becomes reactivated in zoster. Because we do not have any curative antiviral agents for VZV, the goals of therapy are to diminish pain, viral shedding, and duration of symptoms, and to prevent postherpetic neuralgia. There are data that suggest that treating zoster with an antiviral agent in older individuals may prevent post-herpetic neuralgia.[1-3]

Acyclovir (Zovirax) was the first antiviral agent with proven efficacy against VZV. Two newer agents now available are famciclovir (Famvir) and valacyclovir (Valtrex). Preliminary data on these new agents indicate that they are at least as effective as acyclovir for the treatment of zoster.[4] Both newer agents have the advantage of requiring fewer doses per day and currently valacyclovir is priced less expensively than acyclovir and famciclovir.

References

1. Jackson JL, Gibbons R, Meyer G, Inouye L. The effect of treating herpes zoster with oral acyclovir in preventing postherpetic neuralgia. A meta-analysis. *Arch Intern Med* 1997; 157:909-912.
2. Wood MJ, Shukla S, Fiddian AP, Crooks RJ. Treatment of acute herpes zoster: effect of early (< 48h) versus late (48-72 h) therapy with acyclovir and valaciclovir on prolonged pain. *J Infect Dis* 1998; 178:S81-S84.
3. Dworkin RH, Boon RJ, Griffin DR, Phung D. Postherpetic neuralgia: impact of famciclovir, age, rash severity, and acute pain in herpes zoster patients. *J Infect Dis* 1998; 178:S76-S80.
4. Calza AM, Schmied E, Harms M. Systemic corticosteroids do not prevent postherpetic neuralgia. *Dermatology* 1992; 184:314-316.

Does regular exercise during pregnancy affect the physical growth or mental development of infants?

Clapp JF 3rd, Simonian S, Lopez B, Appleby-Wineberg S, Harcar-Sevcik R. The one-year morphometric and neurodevelopmental outcome of the offspring of women who continued to exercise regularly throughout pregnancy. *Am J Obstet Gynecol* 1998; 178:594-599.

QUESTION: What is the effect of regular, sustained, antigravitational exercise during pregnancy on the postnatal growth and neurodevelopment of infants?

Correspondence to:

Dr Clapp 3rd

Department of Obstetrics and Gynecology, MetroHealth Medical Center, 2500 MetroHealth Drive, Cleveland, OH 44109

Design

Cohort study with follow-up at 1 year.

Setting

USA.

Participants

A total of 104 infants of women recruited from an ongoing study of exercise during pregnancy returned for follow-up and had a satisfactory evaluation at 1 year. All mothers had had uncomplicated pregnancies. All mothers were white, 25-38 years old, had family incomes in the upper 50%, had a median of 17 years of education, and most (91%) worked outside of the home. They all had well balanced diets, had 12-28% body fat, and had no chronic illnesses; they did not use tobacco or drugs. Median parity was two. Exclusion criteria were an abnormal antenatal course (premature labor, pregnancy-induced hypertension, abruptio placentae, or intrauterine growth retardation); intrapartum complications (for example, sepsis, fetal distress, or Apgar score <7); and diseases in infancy that could directly affect development (recurrent otitis media with effusion, feeding problems, surgery, or severe or protracted illness).

Assessment of risk factors

Fifty-two mothers were classified as exercisers (they ran, did aerobics, or used stair climbing machines >3 times/week for >20 min at an intensity >55% of their maximal performance during pregnancy), and 52 were classified as physically active (they participated in intermittent activity such as golf, tennis, or hiking; infrequent activity; or no recreational exercise).

Main outcome measures

Within 24 hours of birth, a trained examiner measured the infant's weight; length; head, chest, and abdominal circumference; triceps and subscapular skinfold thickness; and fat mass. Within 1 month of the child's first birthday an examiner who was unaware of the mother's exercise status administered the original Bayley Scales of Infant Development (psychomotor and mental scales), and a different examiner repeated the morphometric measurements.

Main results

At birth, the infants of mothers who had continued exercising during pregnancy had lower birth weights and less body fat (both P=0.05) than infants of mothers who were physically active, but they did not differ in length, head circumference, or lean body mass. At 1 year, the groups did not differ on any of the morphometric assessments or on performance measured by the Bayley mental scale. Infants of women who exercised performed slightly better on the Bayley psychomotor scale (P=0.05).

Conclusion

Regular, sustained, antigravitational exercise during pregnancy did not affect infants' physical growth or mental development at 1 year.

Funding: National Institute of Child Health and Human Development, the Alexander von Humboldt Foundation, MetroHealth Medical Center.

This article was originally published in *Evidence-Based Nursing* 1999; 2:22.

COMMENTARY

Grace Edwards, RGN, RM, ADM, M Ed., Regional Perinatal Surveys Manager, Unit of Perinatal and Pædiatric Epidemiology, University of Liverpool, Liverpool L69 3BX

Research suggests that regular aerobic exercise during pregnancy improves physical fitness, although a systematic review of the available trials found insufficient data to identify important risks or benefits to the mother or infant.[1]

This study by Clapp et al followed a cohort of 104 physically fit women who became pregnant. The women were divided into two groups: those who continued to exercise regularly during pregnancy and those who were physically active but exercised intermittently. It might have been useful to have included a group of women who did not exercise at all.

The lack of confounding variables means that the study is clear, but this makes the findings less generalizable to other groups of pregnant women. Although the findings showed a statistically significant difference in body fat at birth and in the psychometric scores of infants at 1 year, these findings are not clinically significant. No consideration was given to the parity of the women, which may have had an effect on the birth weight of the infants. The authors rightly point out the limitations of a small, non-representative cohort and are aware of the limitations of the Bayley Scales of Infant Development. All intelligence tests have different strengths and limitations and these should be considered carefully before use.

Women who exercise regularly before becoming pregnant may seek advice from nurses and other health professionals on whether to continue exercising during pregnancy. This study will allow clinicians to reassure active women who meet the selection criteria that they can safely continue to be moderately active during pregnancy without harm to the fetus. Large, randomized controlled trials are needed to adequately assess the potential effects of exercise during pregnancy for women and their babies.

[1] Kramer MS. Regular aerobic exercise during pregnancy. In: Cochrane Collaboration, latest version 29 April 1996. Cochrane Library. Oxford: Update Software, 1996.

Are baseline depressive symptoms associated with smoking initiation in adolescents?

Escobedo LG, Reddy M, Giovino GA. The relationship between depressive symptoms and cigarette smoking in US adolescents. *Addiction* 1998; 93:433-440.

QUESTION: Do depressive symptoms at baseline influence the rates and patterns of smoking initiation and cessation at follow up in adolescents?

Design

Inception cohort of adolescents sampled from the community and followed for 4 years in the Teenage Attitudes and Practices Survey (TAPS).

Setting

USA.

Participants

7885 adolescents (51% boys) who were 10-18 years of age at baseline and lived in households selected for the US National Health Interview Survey (last two quarters of 1988 and the first two quarters of 1989) were eligible to participate; 5828 adolescents (53% boys) without depressive symptoms at baseline and 1228 adolescents (60% girls) with depressive symptoms at baseline were analyzed for smoking initiation. A total of 576 smokers (59% boys) without baseline depressive symptoms and 253 smokers (62% girls) with baseline depressive symptoms were analyzed for smoking cessation. Nonsmokers included "puff smokers" (those who had smoked at least one but not 100 cigarettes), former or experimental smokers (those who had smoked >100 cigarettes but had not smoked in the previous month), and occasional smokers (those who had smoked one cigarette and had smoked during <5 days in the previous month).

Assessment of prognostic factors

Race, school performance, risk-taking behavior, age, the presence of smokers in the household, and parental educational level were assessed for potential confounding effects.

Main outcome measures

Number of non-smokers who began smoking regularly (that is, smoked >5 cigarettes in the previous month) and number of regular smokers who stopped smoking (did not smoke in the previous 30 days and did not think they would be smoking 1 year later).

Main results

After adjustment for race, school performance, risk taking, and the presence of smokers in the household, depressed adolescents were more likely than nondepressed adolescents to start smoking regularly (Table 1). No association between depressive symptoms and rates of smoking cessation was seen after further adjustment for age and parental educational level (Table 1).

Table 1 *Association between baseline depressive symptoms and smoking patterns in adolescents*

Outcomes after 4 years (rate)	Adjusted odds ratio (95% CI)
Smoking initiation	1.3 (1.1 to 1.6) [A]
Smoking cessation	0.7 (0.5 to 1.1) [B]

[A] Adjusted for race, school performance, risk-taking behavior, presence of smokers in the household, and region.

[B] Not significant. Adjusted for race, school performance, risk-taking behavior, presence of smokers in the household, region, and parental educational level.

Conclusions

Adolescents who had depressive symptoms at baseline were more likely than those who did not have depressive symptoms to start smoking regularly. No association was seen between depressive symptoms at baseline in adolescent smokers and cessation rates 4 years later.

Funding: National Cancer Institute, American Cancer Society, Robert Wood Johnson Foundation.

This article was originally published in *Evidence-Based Mental Health* 1999; 2:22.

Correspondence to:

Dr Escobedo

New Mexico Department of Health, 1170 North Solano Drive, Suite L, Las Cruces, NM 88001

COMMENTARY

Naomi Breslau, Henry Ford Health Sciences Center, 1 Ford Place , Detroit, MI 48202-3450

Understanding the etiology of smoking, especially in adolescence, is important in preventing or reducing smoking. It is difficult to disentangle spurious causal effects from the true causal effects of suspected risk factors. The study by Escobedo et al achieves this by using a longitudinal design and statistical controls. Escobedo et al reported that symptoms of depression and anxiety at baseline increased the risk of smoking 4 years later. The observed effect, although small, is of considerable importance given the relatively high prevalence of depressive and anxious symptoms among adolescents. Nonetheless, important questions remain. The authors referred to the risk of becoming a regular smoker (that is, of having smoked 5 days during the previous month) as a risk of smoking initiation, a term that indicates smoking for the first time. In one analysis, the authors estimated the risk of regular smoking in adolescents who had been nonsmokers, ever-smokers, or occasional smokers; this analysis combines initiation and progression to regular smoking. In another analysis, they reported the incidence of regular smoking among adolescents who had never smoked, providing a clearer test of the role of depressive symptoms in regular smoking. Had they also reported the combined incidence of any stage of smoking during the 4-year interval, we would be able to gain insight into the effects of depressive symptoms on smoking initiation as distinct from progression to greater involvement.

The importance of this distinction stems from research showing that the initiation and progression of adolescent drug use might be preceded by different conditions. Initiation might result from social influences, such as peer use, whereas progression might be more closely tied to internal states, such as depressed mood. Evidence that major depression is a risk factor for progression to daily smoking has been reported.[1]

Evaluation of the role of emotional distress in adolescents' initiation or progression of smoking should take into account the strong correlation between conduct problems and drug use and emotional distress.[2] The finding that emotional distress, either alone or in conjunction with conduct problems, increases adolescents' vulnerability to smoking cannot be ignored.

1 Breslau N, Peterson EL, Schultz LR, Chilcoat HD, Andreski P. Major depression and stages of smoking: a longitudinal investigation. *Arch Gen Psychiatry* 1998; 55:161-6.

2 Hawkins JD, Catalano RF, Miller JY. Risk and protective factors for alcohol and other drug problems in adolescence and early adulthood: implications for substance abuse prevention. *Psychol Bull* 1992; 112:64-105.

Self-management education for adults with asthma improves health outcomes

Gibson PG, Coughlan J, Abramson M, et al. The effects of self-management education and regular practitioner review in adults with asthma. *Cochrane Collaboration*, latest version 26 Feb 1998. In: Cochrane Library. Oxford: Update Software, 1998.

QUESTION: Is education in self-management plus regular review by clinicians effective in improving health outcomes for adults with asthma?

Correspondence to:

Dr Gibson

Respiratory Medicine, John Hunter Hospital, Locked Bag 1, Hunter Mail Centre, New South Wales 2310, Australia

Data sources

Studies were identified on Medline, EMBASE/Excerpta Medica, and CINAHL using the terms "asthma" or "wheeze" with "education" or "self-management." Bibliographies of studies were scanned, and 16 respiratory journals and meeting abstracts from three specialty societies were hand searched.

Study selection

Controlled trials were selected if most of the patients studied were adults with confirmed asthma; the intervention included education related to asthma and its management; and the outcomes included hospitalization for asthma, visits to emergency departments, unscheduled visits to physicians, days lost from work or school, lung function, use of rescue β agonists or oral corticosteroids, symptom scores, quality-of-life scores, and economic outcomes.

Data extraction

Data were extracted on study quality, patient and disease characteristics, educational interventions, health outcomes, intermediate outcomes (knowledge and skills), type of control, and duration of intervention. Interventions were divided into categories of optimal self-management (a written action plan for self-management of medications for exacerbations, self-monitoring, and regular review); self-monitoring and regular review without a written action plan; self-monitoring only; and regular review only.

Main results

A total of 22 randomized controlled trials met the inclusion criteria (25 studies with 27 interventions). Eight studies provided length of follow-up (range 1 month to 1 year). Self-management led to reductions in the proportion of patients who were hospitalized, had unscheduled physician visits, had days off work or school, and had nocturnal asthma (Table 1).

Table 1 *Self-management education compared with usual care for adults with asthma*

Outcomes	Weighted event rates		RRR (95% CI)	NNT (CI)
	Self-management	Usual care		
Hospitalization	6.9%	9.7%	38% (6 to 59)	38 (20 to 382)
Unscheduled physician visits	28.9%	37.4%	26% (10 to 39)	12 (8 to 36)
Days off work	36.6%	51.8%	25% (10 to 37)	7 (5 to 13)
Nocturnal asthma	28.8%	37.7%	30% (17 to 41)	12 (8 to 23)

RRR=relative risk reduction; NNT=number needed to treat.

Optimal self-management generally resulted in greater reductions and was associated with improved lung function. A written action plan was associated with fewer hospital admissions. Five studies compared optimal self-management with physician-managed care, and outcomes did not differ.

Conclusions

Patients with asthma who are given self-care management education have a lower incidence of hospitalization, unscheduled physician visits, days off work, and nocturnal asthma. Reductions are greater when the self-management education includes a written care plan.

Funding: NSW Health Australia and National Asthma Campaign Australia.

COMMENTARY

Peter K Honig, Office of Drug Evaluation, Food and Drug Administration, CDER Pulmonary Group, 5600 Fishers Lane, Rockville, MD 20857

Until recently, the randomized controlled trial was the gold standard for evaluating therapeutic interventions. Now meta-analyses have gained acceptance among practicing healthcare providers as a method for quantitatively summarizing evidence to assist in medical decision-making. This meta-analysis by Gibson and colleagues shows that optimal asthma self-management consisting of a written action plan for the use and adjustment of medication, self-monitoring of asthma symptoms and airflow, and regular review of these activities by the managing caregiver results in greater clinically significant improvements in several outcomes.

What message should practitioners who manage patents with asthma take from these findings? Most guidelines acknowledge and emphasize the importance of the strategies reviewed by Gibson and colleagues.[1] This systematic review helps to quantify the relative benefits of patient education and directed self-management techniques in the treatment of patients with asthma. It provides persuasive evidence of the value added by various interventions, including written action plans, for the provider of asthma care to consider when allocating limited time and resources.

Asthma prevalence and mortality are continuing to increase. Reducing hospital admissions, office visits, and other indices of asthma control are important both to patients and to caregivers. This well done meta-analysis confirms the value of optimal asthma self-management and validates the published guideline recommendations for such interventions.

1 National Heart, Lung, and Blood Institute. *Guidelines for the Diagnosis and Management of Asthma*. Bethesda: National Institutes of Health, 1997. US Department of Health and Human Services, publication number 97-4051.

Older adolescents discuss sexual behavior with partners after trust has been built

Lock SE, Ferguson SL, Wise C. Communication of sexual risk behavior among late adolescents. *West J Nurs Res* 1998; 20:273-294.

QUESTION: How do older adolescents perceive communication with their partners about sexual risk behavior (multiple partners; sexual intercourse without condoms; or sexual intercourse with partners who are infected with HIV, have a sexually transmitted disease (STD), or who use or have used intravenous drugs)?

Design

Grounded theory.

Setting

A public university in the southeast United States.

Participants

32 single adolescents (mean age 19 years, 56% women, 72% white, and mean age at first intercourse 17 years) who had never been pregnant or fathered a child and who had had sexual intercourse.

Methods

A semistructured interview was conducted by a researcher of the same sex. The interview dealt with perceptions of decisions to have sexual intercourse and discussions with partners about birth control, previous sexual partners, STDs, and intravenous drug use. Interviews were analyzed separately for men and women using constant comparative analysis.

Main findings

Building trust was the core variable. Both men and women were more comfortable talking about sexual risk behavior when they trusted their partners. Women built trust by gathering information indirectly about potential sexual partners, and men used their instincts and assessed external factors. After trust was established, women felt that they could initiate discussions on sexual risk behavior, and men felt that they were willing to take part in discussions. Women felt that open discussions were easier if alcohol was not used; if they had had previous sexual experience and had a good knowledge base about reproduction, contraception, and sexual risk behavior; if they had discussed similar topics with their friends; or if the media had provided the motivation to discuss sexual risk-related topics. Men and women felt trust had to be shown repeatedly. Despite talking about safe sex, many participants showed trust in their partners by engaging in unsafe sexual practices.

Conclusions

Older adolescents felt willing and able to discuss sexual risk behavior when they were in a stable relationship after trust had been established. Discussion did not guarantee safe sexual behavior.

Funding: American Nurses Foundation.

This article was originally published in *Evidence-Based Nursing* 1999; 2:27.

Correspondence to:

Dr Lock

College of Nursing, University of Kentucky, 435a Health Sciences Learning Center 0232, Lexington, KY 40536-0232

COMMENTARY

Lynn Rew, Associate professor and graduate adviser, School of Nursing, University of Texas at Austin, 1700 Red River, Austin, TX 78701

Lock et al provide an interesting new model of the communication of sexual risk behavior among adolescent partners. Most participants had used condoms during the last time they had intercourse and seemed to be knowledgeable and generally conscientious about safe sex practices.

What is particularly useful about this model is that it shows the differences in the way that young men and women approach communication with potential sexual partners about safe sex practices. Although both agreed that a caring relationship was needed to gain confidence that a potential sexual partner was being truthful about sexual history, women were more likely to initiate a conversation about safe sex and to identify circumstances that influenced such talks. Women were frustrated with having to initiate discussions and were discouraged when partners either did not continue the discussion or became angry. This suggests that young women carry a heavy burden for protecting themselves and could benefit from learning assertiveness strategies.

Among women, the findings that alcohol clouds judgment, and that previous sexual experience, knowledge about sexual issues, social support, and messages from the media increased their likelihood of engaging in discussions of safe sex should form the basis for safe sex interventions. We do not know how such interventions might influence the communication behaviors of men.

A recent publication in the United States focuses on topics in sexuality education that are difficult to teach, such as negotiating safer sex.[1] Most teachers admit that they do not know how to encourage young adolescents to assess their sexual risk, to set limits, or to avoid mixing alcohol and drugs with sexual activity. If further research shows that this model is also applicable to younger teenagers, it may provide direction for nurses, other professionals, or parents to develop and test more effective strategies to help teenagers negotiate safe sex.

[1] Sexuality Information and Education Council of the United States. Filling the gaps: hard to teach topics in sexuality education. New York: SIECUS; 1998.

Best Practice

EVIDENCE-BASED CASE REVIEW

Heart failure: Part I. First hospitalization and post-hospital care

Objectives of this Evidence-based Case Review

- Understand the importance of a focused diagnostic work-up of heart failure
- Understand the etiologies of heart failure
- Recognize the treatments available and understand which have been shown to improve quality or quantity of life
- Understand the impact of heart failure on society
- Understand the criteria for hospitalization and reasons for readmission

Michael S Wilkes
General Internal Medicine and Health Services Research

Holly Middlekauff
Division of Cardiology

Jerome R Hoffman
Emergency Medicine Center
University of California
Los Angeles, CA

Correspondence to:
Dr Wilkes
mwilkes@ucla.edu

Conflicts of Interest:
None declared.

Introduction

American medicine has made great strides in the reduction of death from acute myocardial infarction (MI). This success in primary prevention (preventing the disease from occurring) has been matched with successes in secondary prevention (preventing more serious complications once the disease occurs). As we move into the next century, more people are living to older ages and more people survive myocardial infarctions, so the burden has now shifted to the management of a chronic disease—namely heart failure. Heart failure accounts for more hospitalizations in the elderly than any other cause, and is the only major cardiovascular disorder whose incidence and prevalence are increasing. An estimated 400,000 new cases of heart failure occur each year, adding to the 5 million Americans who have already been diagnosed with a failing heart.[1] Approximately 250,000 people die each year from heart failure, and experts feel that death certificates and other vital statistics underestimate the incidence. The average mortality rate is 10% at 1 year and 50% after 5 years.[1] In addition, many heart failure patients experience a poor quality of life due to uncomfortable physical symptoms, depression, and reduced functional status. Because the incidence of heart failure rises substantially beyond age 65, the prevalence of this condition will rise as the population ages.

Society also suffers under the burden of the ailing heart. The treatment of heart failure consumes more than $10 billion in health care expenditures each year. This figure could be decreased, and the rate of hospitalizations decreased, by improved outpatient care, focusing on appropriate interventions that have been shown to improve either the quality or quantity of life, and eliminating those tests and treatments that are of dubious value. In this evidence-based case review, we present the case of Mr. G., a man with a typical presentation of chronic congestive heart failure.

Mr G. is a 60-year-old recently retired security guard. Besides mild (160-170) systolic hypertension, being 15% overweight, and getting relatively little exercise, Mr. G. had been in good health until one month ago when he suffered an uncomplicated anterior wall myocardial infarction. He is now being discharged after a 5-day hospitalization.

What post-hospital care and follow-up does Mr. G. need?

Initially our treatment goals include maximizing cardiac function, improving quality of life, and decreasing mortality. According to the evidenced-based AHCPR guidelines, most patients who have recently had an MI can benefit from an echocardiogram, unless they are at low risk for systolic dysfunction. Low risk patients include those with no previous MI, or with a small uncomplicated MI (involving the inferior wall, with relatively small rise in enzymes, without Q waves on ECG, and with an uncomplicated clinical course [i.e. without arrhythmias or hypotension]). Most other patients should obtain M-mode, two-dimensional, and Doppler echocardiograms, and an imaging study to assess for undetected ischemia.

Doppler is useful for diagnosing left ventricular diastolic dysfunction and valvular disease. The two-dimensional echocardiogram measures LV ejection fraction and other cardiac function parameters along with chamber size, wall thickness, and functional changes due to ischemia or infarction. The cost of the two tests varies, but averages around $600. Patients in whom one can identify valvular disease may benefit from early surgical intervention, and those with a normal LVEF should be monitored closely when taking diuretics, so as to maintain proper LV filling pressures.[2]

Mr. G.'s echo shows a moderately reduced left-ventricular systolic function (ejection fraction= 40%). His valvular function is normal.

What interventions are necessary at this point?

Mr. G. and his family need counseling about the meaning of heart failure, drug regimens, dietary restrictions, symptoms of worsening heart failure, what to do if these symptoms occur, and prognosis. Quality of life in patients with heart failure may be related as much to the psychological state as to the disease and its resultant limitations. Allied health interventions, family understanding and involvement, and support groups may help patients cope with heart failure. Because of the large number of issues that need to be addressed, it may be useful to seek the assistance of other experts including

dietitians, nurse educators, clinical nurse specialists, and pharmacists.

Mr. G. should be told to obtain a bathroom scale and to weigh himself each morning (after urinating and before eating). He will need to contact us if his weight has changed by more than 4 pounds since the last clinical evaluation. One common approach is to educate patients that if they gain more than 3-4 pounds over a couple of days they should increase their diuretic dose prior to contacting their doctor. Mr. G. should understand that he may feel tired and that sexual difficulties are common in persons with heart failure. Sexual behaviors may need to be altered due to limited exercise tolerance. We should not expect Mr. G. to bring up these issues but rather we should bring up these topics and discuss them openly. Further, Mr. G. should be up-to-date on his immunizations (influenza and pneumococcus) and be told about the importance of not smoking or chewing tobacco, and about the importance of regular limited exercise.

Can patients with heart failure be classified in terms of their disease and prognosis?

In order to classify the severity of symptoms in patients with heart failure, the New York Heart Association developed a four-level scheme that is often criticized as unreliable, yet is still used in many of the studies that are discussed below. Therefore it is prudent to review these four levels:

- I Cardiac disease without resulting limitations of physical activity;
- II Slight limitation of physical activity—comfortable at rest, but ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain;
- III Marked limitation in physical activity—comfortable at rest, but less than ordinary physical activity causes fatigue, palpitation, dyspnea, or anginal pain;
- IV Inability to carry on any physical activity without discomfort, or symptoms occur at rest.

Clinical features that are associated with more favorable prognosis include New York Heart Association class I to class II symptoms, younger age, and female gender. Syncope, a persistent third heart sound, signs of chronic right-sided heart failure, extensive conduction system disease, and ventricular tachyarrhythmias portend a poor prognosis. Progressive heart failure accounts for the majority of deaths.

Researchers have also tried to correlate physiologic variables (e.g., peak oxygen uptake, peak VO_2 and exercise-induced age-adjusted peak oxygen uptake), with patient outcomes. Unfortunately, obtaining these measurements in heart failure patients is expensive and time consuming. A simple means of assessing severity of disease and left ventricular dysfunction in patients with heart failure is the 6-minute walk.[3, 4] Patients are asked to walk a 30-meter path for a total of 6 minutes. Patients walk at their own pace and received oral encouragement from a nurse every 30 seconds. The longer the distance walked, the better the 4-month prognosis. In the previous studies, those walking less than 300 meters had a mortality of 10% compared with 3% for those walking more than 450 meters.

In the absence of any symptoms, what medications, if any, should Mr. G. take?

Aggressive control of blood pressure, ACE inhibitors, reduction of LDL to below 100, aspirin, beta blockers, and the avoidance of antiarrythmics, other than possibly amiodarone, can significantly reduce stroke, myocardial infarction, and the incidence of heart failure. Researchers reviewed studies of more than 26,000 patients with hypertension. Those who were treated actively with antihypertensives had a 1.6% chance of progressing to heart failure compared to 3.4% for the untreated group.[5-7] At least one study (pharmaceutical manufacturer sponsored) makes a compelling case that there is added value from using an ACE inhibitor as the first-line antihypertensive therapy for patients with systolic hypertension and left ventricular dysfunction.[8]

As a result of a decreased cardiac output in heart failure, there is increased sympathetic tone that triggers the renin-angiotensin system. The activation of this system leads to a further increase in sympathetic tone an increase in aldosterone, and retention of water and sodium. The net result is an increase in afterload. The goal of ACE inhibitor therapy is to break this cycle. ACE inhibitors (enalapril or captopril and possibly others) block angiotensin II production.[9-15] Currently, experts recommend starting ACE inhibitors on all patients with left-ventricular dysfunction, regardless of symptoms. While most of the research on ACE inhibitors in heart failure patients has investigated captopril and enalapril (the only two approved by the FDA for this indication), other ACE inhibitors, e.g., lisinopril, appear to be equally effective and associated with no additional side effects. [16]

A series of high-quality randomized clinical trials have shown that the ACE inhibitors are the first group of drugs to decrease mortality. Enalapril reduces mortality more than the combination of isosorbide dinitrate and hydralazine.[10] In the CONSENSUS trial, which studied only patients with NYHA Class IV heart failure, 1-year mortality was reduced from 52% with placebo to 36% with enalapril. The degree of benefit is more modest in the general heart failure population. SOLVD suggests that median survival for patients with ACE inhibitors actually increased by approximately 6 months.

Contraindications to the use of ACE inhibitors include elevated serum potassium (>5.5 mEq/L) or symptomatic hypotension. Those with elevated creatinine

(greater than 3.0 mg/dL) should be given a reduced dose of ACE inhibitor and be closely monitored.

A recent manufacturer-supported study suggests that losartan (a specific angiotensin II antagonist that does not increase bradykinin levels) is as effective as the other ACE inhibitors and maybe associated with fewer side effects, although ACE inhibitors as a class are well tolerated.[17] More research is needed to see whether these newer agents offer significant clinical advantages.

Several double-blind, controlled studies compared the effects of an ACE inhibitor (enalapril 10 mg bid—if tolerated) on patients with heart failure and ejection fractions less than 35%. There was a significant slowing of disease progression and a reduction in hospitalizations. Subgroup analysis suggests that those who would benefit most from ACE inhibitors are those with lower initial ejection fractions. This study and others have established that patients with heart failure should be placed on ACE inhibitors as early as possible after the diagnosis is made.[18-21] Therefore, Mr. G. should start an ACE inhibitor despite his mild symptoms.

Despite the consistent research evidence of the benefits of ACE inhibitors in treating heart failure, up to 60% of patients are not provided with these drugs. Furthermore, many patients for whom ACE inhibitors are prescribed are given far smaller doses than recommended (recommended dose: 10 mg BID of enalapril, 10 mg per day of lisinopril, 50-100 mg BID for captopril).[22-28]

If we start Mr. G. on an ACE inhibitor, what should we monitor?

Monitor blood pressure, renal function, and potassium levels. Side effects include cough, renal dysfunction, hypotension, and angioedema. Cough affects 5-10% of people (more often women), and is unrelated to the type of ACE inhibitor used. It is self-limiting, and usually stops within a few days of stopping the drug. The proposed mechanism of action is a potentiation of bradykinin and prostaglandin levels, which cause bronchial reactivity.[29]

Angioedema is a potentially life-threatening complication that requires prompt recognition and withdrawal of the agent. The incidence of this side effect is 0.1 to 0.2%. Although most cases are mild, deaths have occurred. Angioedema, which may not have an allergic etiology (since it is not associated with pruritis and urticaria), most commonly occurs during the first week of treatment, but it can occur within hours of, or as late as years after, institution of therapy. Angioedema can occur in association with any of the agents, despite the differences in their chemical structure.[30, 31]

In terms of potassium, one large retrospective study looked at 194 patients, half of whom had developed hyperkalemia. Risk factors for hyperkalemia included an increase in BUN, creatinine (higher than 1.6 mg/dL), and the use of a long-acting ACE inhibitor (such as lisinopril or enalapril), while concomitant use of a loop or thiazide diuretic was associated with a reduced risk of hyperkalemia.[32]

Mr. G. did well for 6 weeks, then he noticed some swelling around his ankles, mild shortness of breath when he walked from his home to the mailbox, and near constant fatigue. Since the time of his discharge he has not experienced any chest pain. He reports that he takes his medicines regularly.

How would you proceed with Mr. G.'s workup? Are there other items from the history that you would like to know?

At this point one needs to consider reversible causes of heart failure, including anemia, another MI, pulmonary disease, arrhythmias, renal failure, and thyroid disease. Many of these are correctable. One should carefully review his medications to make sure he is not taking any cardiac depressants.

What parts of the history and physical examination would prove useful in either ruling in or excluding disease?

In addition to organ system–related questions (orthopnea, paroxysmal nocturnal dyspnea, dyspnea on exertion, syncope or near syncope, and new onset palpitations) a complete history should include questions regarding physical functioning, mental health, sleep disturbance, sexual function, cognitive function, ability to perform usual work, and social activities. You should determine and chart the most strenuous activity that Mr. G. can perform. Activities should be defined in terms of usual activities, e.g., walking (with attention to distance, pace, and grade), stair climbing, or activities of daily living (e.g., bathing, dressing). Once these are determined, they are useful indicators to monitor progress from visit to visit. Family members often provide additional information about patients status and compliance.

A careful physical examination with particular attention to the cardiac, vascular, and pulmonary system is needed. An effort should be made to assess signs of volume overload including jugular venous distension (JVD), third heart sound, rales, dyspnea on exertion (objective assessment), hepatic engorgement, hepatojugular reflux, ascites, and peripheral edema. However, the physical examination is not sensitive for diagnosing heart failure and thus is poor at ruling out heart failure. Similarly, most physical findings are not specific for heart failure and thus are poor at ruling in disease. Of the physical findings listed, elevated JVP and a third heart sound are the most specific and, in the presence of a compatible history, can be considered diagnostic.

Table 1 *Recommended Tests for Patients With Signs or Symptoms of Heart Failure*

Test Recommendation	Finding	Suspected Diagnosis
Electrocardiogram	Acute ST-T wave changes, atrial fibrillation, other tachyarrhythmia	Myocardial ischemia, thyroid disease or heart failure due to rapid ventricular rate
	Bradyarrhythmias	Heart failure due to reduced left-ventricular performance
	Previous MI (e.g., Q waves)	Heart failure due to reduced left-ventricular performance
	Low voltage	Pericardial effusion
	Left-ventricular hypertrophy	Diastolic dysfunction
Complete blood count	Anemia	Heart failure due to or aggravated by decreased oxygen-carrying capacity
Lipids	Increased LDL and decreased HDL	Hypercholesterolemia
	Red blood cells or cellular casts	Glomerulonephritis
Serum albumin	Decreased	Increased extravascular volume due to hypoalbuminemia
T_4 and TSH (obtain only if atrial fibrillation, evidence of thyroid disease, or patient age>65)	Abnormal T_4 or TSH	Heart failure due to or aggravated by hypo/hyperthyroidism

Modified from AHCPR

A well-proven relationship exists between physical signs and hemodynamic functions for acute congestive heart failure; in chronic congestive heart failure, however, compensatory mechanisms make the physical examination unreliable.[33] Pulmonary rales, hepatic engorgement, ascites, and peripheral edema are nonspecific physical findings. If there are other explanations for these findings a work-up of heart failure is not indicated. The low inter-rater reliability of physical findings such as rales and a third heart sound[29,34] emphasizes the need for careful examination. However, the poor predictive value of physical findings reported in the literature should be interpreted cautiously, because these studies evaluated patients at a single point in time. Although the presence or absence of a third heart sound does not make or exclude the diagnosis of heart failure, if a patient with heart failure develops a new third heart sound or rales, it is likely that this patient's heart failure has worsened. Thus, physical examination may be more helpful in following patients with heart failure than in making a diagnosis.

Mr. G. has some paroxysmal nocturnal dyspnea and he has been sleeping with three pillows—two more than usual. He is also experiencing some dyspnea on exertion. His blood pressure is 150/88.

What tests would you perform at this point and how will they alter your management of Mr. G.?

The above chart from the AHCPR (Table 1) is a useful synopsis of tests indicated in the presence of various signs and symptoms of CHF.

Given that Mr. G. has a history that is consistent with heart failure, it would be wise to reassess left ventricular performance. The combined use of history, physical exam, CXR and EKG does a poor job at differentiating between dilated cardiomyopathy, valvular disease, left ventricular diastolic dysfunction or non cardiac etiology. Therefore, it would make sense to order a repeat ECHO or radionuclide ventriculography, and possibly a treadmill exercise test or other study, to assess the possibility of coronary ischemia. A chest x-ray is helpful in determining signs of cardiac failure, the presence of a pleural effusion, or any indications of chronic pulmonary, infectious or malignant processes. An ECG can provide information regarding arrhythmias, ventricular hypertrophy, and conduction abnormalities. In a study of patients who had been referred for echocardiography, 19% had evidence of LV systolic dysfunction, of whom the great majority (90%) had major EKG abnormalities, and none had a completely normal EKG. Conversely, 39% of patients with a normal echo had an abnormal ECG. Thus the sensitivity (the percentage of patients with the problem [in this case systolic dysfunction] who had an abnormal test [in this case the EKG]) and specificity (the percent-

age of patients without the problem who had a normal test) of a major ECG abnormality in predicting LV dysfunction were 94% and 61%, respectively.

The positive predictive value (the probability of someone with an abnormal EKG having LV dysfunction) and negative predictive values (the probability of someone with a normal EKG having no LV dysfunction) were 35% and 98%. Because valvular disease may exist in the face of a normal EKG, an echocardiogram should still be done, regardless of EKG findings, in patients with a suspicious murmur.[7]

In terms of laboratory tests, a CBC is useful to evaluate for anemia and infection. Serum creatinine would help determine if fluid overload is secondary to renal failure. Thyroid stimulating hormone (TSH) is more controversial. In someone younger than 65 TSH is probably not indicated in the absence of other physical findings suggestive of thyroid disease (e.g., atrial fibrillation).

At what point would you consult a cardiologist?

The choice of when to obtain a consultation is an individual one, that should be based in part on the primary care giver's comfort level and in part on the condition of the patient. There are no studies to guide this decision, although many published reports have shown that cardiologists are more likely than generalists to apply recent findings, and published guidelines, to individual patient care.

Is there a reason to assess Mr. G.'s serum magnesium concentration?

It may be useful to measure serum Mg concentrations in CHF; some case-control studies have shown that patients with a low Mg level have a worse prognosis than those with a normal level. Research suggests that inpatients with low serum levels and chronic stable heart failure IV, magnesium appears to decrease ventricular arrhythmias. It is important to note, however, that while PVCs decrease, the number of PVCs is not of clinical importance, and there was no change in the incidence of ventricular tachycardia.[35] In the only RCT to date, in fact, serum magnesium was not a predictor of mortality in patients with moderate to severe heart failure.[36] Checking electrolytes (including magnesium) makes most sense in patients who are taking diuretics. In the absence of conclusive data, we feel that it is reasonable to check magnesium concentration, and maintain normomagnesemia, in patients who are taking diuretics.

The radiographic findings are consistent with left ventricular failure. Mr. G. had bilateral pulmonary vascular congestion and pulmonary edema with small bilateral effusions. CBC, creatinine, liver function tests, serum albumin and electrolytes are all normal. The ECG shows LVH with a normal sinus rhythm. The echo shows an EF of 35%.

Would you hospitalize Mr. G.?

Our goal for Mr. G. is to maximize both his quality of life and the length of his life. Some interventions can be conducted at home including a trial of new medications, a low salt diet, and physical therapy, but we would hospitalize our patient for a short period to adjust the diet, provide patient education and close monitoring, and maximize the chances that he will comply with the proposed life style changes. The AHCPR guideline suggests that any of the following are indications for hospitalizing our patient.

- **ECG evidence of acute myocardial ischemia**
- **Unable to manage at home**
- **Failure of outpatient management**
- **Anasarca**
- **Complicating medical illness (e.g., diabetes, pneumonia)**
- **Evidence of poor oxygenation (oxygen saturations below 90%) that is not explained by pulmonary disease**
- **Hypotension or syncope**

In short, patients at high risk for poor outcomes should also be hospitalized. Studies looking at predictors of outcomes include one which followed 435 patients admitted urgently with heart failure. Factors that turned out to predict poor outcome included systolic BP less than 90, a respiratory rate greater than 30, low serum sodium level, and recent ST- or T-wave changes not attributable to digitalis. Predictors of poor outcomes identified by other research include older age, intraventricular conduction disturbances, elevated creatinine, and high doses of diuretics.[37] Keeping these factors in mind may further help decide who should be hospitalized because of a high risk of complications.[38]

Are there other criteria that you need to consider when deciding to hospitalize Mr. G.?

You might want to talk with Mr. G. about his preferences, the risks and benefits of hospitalization, and his finances. What will his insurance cover (he does not yet have Medicare)? Mr. G. might be responsible for a large deductible and co-payment, and he may have higher costs if he goes directly to an emergency room than if he presents to his primary care doctor. Managed care patients are more likely to be admitted through an emergency room than are patients with other types of insurance, although length of hospital stay is equivalent for all types of insurance.[39]

Mr. G. is admitted to the hospital. He is educated about his condition. His EF is now 35%, but there is no evidence of an arrhythmia, ischemia or valvular disease, and his laboratory tests are all normal.

References

1. Yusuf S, Thom T, Abbott RD. Changes in hypertension treatment and in congestive heart failure mortality in the United States. *Hypertension* 1989; 13 (suppl5):174-179.
2. Davie AP, et al. Value of the electtocardiogram in identifying heart failure due to left ventricular systolic dysfunction. *BMJ* 1996; 312:222.
3. Bittner V, et al. Prediction of mortality and morbidity with a 6-minute walk test in patients with left ventricular dysfunction. JAMA 1993; 270:1702.
4. Cahalin LP, et al. The six-minute walk test predicts peak oxygen uptake and survival in patients with advanced heart failure. *Chest* 1996; 110:325.
5. Moser M, et al. Prevention of disease progression, left ventricular hypertrophy and congestive heart failure in hypertension treatment trials. *J Am Coll Card* 1996; 27:1214.
6. Levy D, et al. The progression from hypertension to congestive heart failure. *JAMA* 1996; 275:1557.
7. Kostis JB, et al. Ptevention of heart failure by antihypertensive dtug treatment in oldet persons with isolated systolic hypertension. *JAMA* 1997; 278:212.
8. Kostis JB. The effect of enalapril on mortal and morbid events in patients with hypertension and left ventricular dysfunction. *Am J Hyperten* 1995; 8:909.
9. Pfeffet MA, et al. Effect of captopril on mortality and morbidity in patients with left ventricular dysfunction after myocardial infarction. *N Engl J Med* 1992; 327:669.
10. Kleber FX, et al. Impact of convetting enzyme inhibition on progression of chronic heart failute: Results of the munich mild heart failure trial. *Br Heart J* 1992; 67:289.
11. DiBianco R, A large-scale trial of captopril for mild to moderate heart failure in the primary care setting. *Clin Cardiol* 1991; 14:676.
12. Anges K, et al. Efficacy and safety of intravenous captoptil in congestive heart failure. *Curr Ther Res* 1993; 53:167.
13. Garg R, et al. Overview of randomized trials of angiotensin-converting enzyme inhibitors on mortality and motbidity in patients with heart failure. *JAMA* 1995; 273:1450.
14. Davies RF, et al. Enalapril versus digoxin in patients with congestive heart failure: A multicenter Study. *J Am Coll Cardiol* 1991; 18:1602.
15. Fonarow G, et al. Effect of ditect vasodilation with hydralazine versus angiotensin-converting enzyme inhibition with captopril on mortality in advanced heart failute: The Hy-c trial. *J Am Coll Cardiol* 1992; 19:842.
16. Zannad F, et al. Comparison of treatment with lisinopril vetsus enalapril for congestive heart failure. *Am J Cardiol* 1992; 70:78C.
17. Pitt B, et al. Randomised ttial of losartan vetsus captopril in patients over 65 with heart failure (evaluation of losartan in the elderly study, elite). *Lancet* 1997; 349:747.
18. The SOLVD Investigators. Effect of enalapril on mortality and the development of heart failute in asymptomatic patients with teduced left ventticular ejection fractions. *N Engl J Med* 1992; 327:685.
19. Pouleur, H, Results of the treatment ttial of the studies of left ventricular dysfunction (SOLVD). *Am J Cardiol* 1992; 70:135C.
20. Kjekshus J. Effects of enalaptil on long-term mortality in sevete congestive heart failure. *Am J Cardiol* 1992; 69:103.
21. The SOLVD Investigatots, Effect of enalaptil on survival in patients with teduced left ventricular ejection fractions and congestive heart failute. *N Engl J Med* 1991; 325:293.
22. Luzier AB, et al. Impact of angiotensin-converting enzyme inhibitor underdosing on rehospitalization rates in congestive heart failure. *Am J Card* 1998; 82:465.
23. Gattis WA, et al. Is optimal angiotensin-converting enzyme inhibitor dosing neglected in elderly patients with heart failure. *Am Heart J* 1998; 136:43.
24. Clark AL, et al. Sevetity of heart failure and dosage of angiotensin converting enzyme inhibitors. *Br Med J* 1995; 310:973.

Key Clinical Points

- Most patients with chronic heart failure should be taking an ACE inhibitor, diuretic, digitalis, and possibly a beta blocker.
- The care of the patient with heart failure is best accomplished through a team approach with key members, including a pharmacist, dietitian, nurse specialist, occupational therapist, and physician.
- When patients are involved in decision-making and educated about self management, both outcomes and patient satisfaction improve.

25. Mendelson G, et al. Underutilization of angiotensin-convetting enzyme inhibitors in older patients with q-wave anterior myocardial infarction in an academic hospital-based geriatrics practice. *J Am Ger Soc* 1998; 46:751.
26. Stafford RS, et al. National patterns of angiotensin-converting enzyme inhibitor use in congestive heart failute. *Arch Intern Med* 1997; 157:2460.
27. Batt BA, et al. Reasons for underuse of angiotensin-convetting enzyme inhibitors in patients with heart failure and left ventricular dysfunction. *Am J Cardiol* 1997; 79:1118.
28. Philbin EF, et al. Patterns of angiotensin-converting enzyme inhibitor use in congestive heart failute in two community hospitals. *Am J Cardiol* 1996; 77:832.
29. Martinez EJ, et al. Respiratory tract side effects of angiotensin convetting enzyme inhibitors: Current knowledge. *South Med J* 1991; 84:1343.
30. Adkinson NF. Drug allergy. *JAMA* 1992; 268:771-773.
31. Thompson T, Frable MA. Drug-induced, life-threatening angioedema revisited. *Laryngoscope* 1993; 103:10-12.
32. Reardon LC, et al. Hyperkalemia in outpatients using angiotensin-converting enzyme inhibitots: How much should we worry? *Arch Intern Med* 1998; 158:26.
33. Stevenson LW, Petloff JK. The limited reliability of physical signs for estimating hemodynamics in chronic heart failure. *JAMA* 1989; 261:884-888.
34. Sackner-Bernstein JD, et al. Rationale for treatment of patients with chronic heart failute with adtenergic blockade. *JAMA* 1995; 274:1462.
35. Gottlieb SS, et al. Effects of intravenous magnesium sulfate on arrhythmias in patients with congestive heart failure. *Am Heart J* 1993; 125:1645.
36. Eichhorn EJ, et al. Clinical and prognostic significance of serum magnesium concentration in patients with severe chronic congestive heart failute: The promise study. *J Am Coll Cardiol* 1993; 21:634.
37. Brophy JM, et al. Long term prognosis of patients presenting to the emergency toom with decompensated congestive heart failute. *Can J Cardiol* 1994; 10:543.
38. Chin MH, et al. Cortelates of major complications or death in patients admitted to the hospital with congestive heart failure. *Arch Intern Med* 1996; 156:1814.
39. Ni H, et al. Managed care and outcomes of hospitalization among elderly patients with congestive heart failure. *Arch Intern Med.* 1998; 158:1231.

Next month's evidence-based case review will focus on selection of medications for the rehospitalized patient with heart failure in need of treatment modification.

CLINICAL EVIDENCE

Recurrent cystitis in nonpregnant women

This article comes from *Clinical Evidence*, a new resource for clinicians produced jointly by the BMJ Publishing Group and the American College of Physicians-American Society of Internal Medicine. *Clinical Evidence* is an extensively peer-reviewed publication that summarizes the best available evidence on the effects of common clinical interventions gleaned from thorough searches and appraisal of the world literature. The first issue will be available in book form in the UK in June with a US version planned for publication in October. The second issue will be updated and expanded to cover more topics and questions and will be published six months later. Please see the advertisement for more information or alternatively visit our web site at www.evidence.org.

Lisa D Chew

Stephan D Fihn

Department of Obstetrics and Gynecology and the Division of General Internal Medicine, University of Washington, Harborview Medical Center, 325 9th Avenue, Box 359780, Seattle, WA 98104

Correspondence to:
Dr. Chew
lchew@washington.ecu

QUESTIONS: How can you prevent further recurrence in women experiencing at least two infections per year? When should you investigate for urinary tract abnormalities?

INTERVENTIONS

Beneficial
Continuous antibiotic prophylaxis
Postcoital antibiotic prophylaxis
Self-treatment with antibiotics

Likely to be beneficial
Long-term antibiotic prophylaxis

Unlikely to be beneficial
Routine investigation of the urinary tract

Definition
Cystitis is an infection of the lower urinary tract causing dysuria, frequency, urgency, hematuria, or suprapubic pain. Pyuria and bacteriuria are almost always present. The presence of fever, flank pain, nausea, or vomiting suggests pyelonephritis.

Recurrent cystitis may be either a reinfection (after successful eradication of infection) or a relapse after inadequate treatment.

Incidence/prevalence
The incidence of cystitis among premenopausal sexually active women is 0.5-0.7 infections/person year.[1] Between one- and two-fifths of women will experience cystitis during their lifetime. Of these women, 20% will have a recurrence, almost all of which (90%) will be caused by reinfection rather than relapse. Rates of infection fall during the winter months.[2]

Etiology
Cystitis is caused by uropathogenic bacteria in the fecal flora that colonize the vaginal and periurethral introitus and ascend the urethra into the bladder. Prior infection, sexual intercourse, and exposure to vaginal spermicide are risk factors for developing cystitis.[3,4]

Prognosis
There is little evidence on the long-term effects of untreated cystitis. One study found that progression to upper urinary tract infection was infrequent and that most cases of cystitis regressed spontaneously, although symptoms sometimes persisted for several months.[5] Women with a baseline rate of more than two infections per year, over many years, are likely to continue to have recurrent infections.[6]

Aims
To prevent recurrent infection in women predisposed to frequent infections, with minimal adverse effects.

Outcomes
Rate of infection based on urine culture and symptoms.

Methods
We searched Medline for articles published from 1970 to 1998. We reviewed all systematic reviews and RCTs that compared different forms of prophylaxis or prophylaxis versus placebo in nonpregnant women with a history of recurrent cystitis. We excluded studies in populations consisting mainly of men or pregnant women.

Summary Points

- Consistent evidence from RCTs shows that antibiotic prophylaxis (either continuous or postcoital), using trimethoprim TMP-SMZ, nitrofurantoin, or a quinolone, reduces infection rates in women with high rates of recurrent cystitis (at least two per year).
- Limited evidence suggests that intermittent patient-administered treatment (taken at the onset of symptoms) is an effective alternative management strategy to continuous antibiotic prophylaxis in women with high rates of infection (at least two per year).
- Limited evidence suggests that long-term prophylaxis is likely to benefit women with a baseline rate of more than two infections per year over many years. However, long-term treatment has not yet been evaluated in RCTs.
- In women who experience recurrent, uncomplicated cystitis, there is no evidence to support routine investigation of the urinary tract with excretory urography, ultrasonography, cystoscopy, or voiding cystourethrography. No specific subgroups of women who would clearly benefit from investigation have yet been adequately defined.

Table 1 *Continuous antimicrobial prophylactic regimens for recurrent urinary tract infections: results of RCTs*

Study	Number of participants	Regimen	Duration of prophylaxis	Infections/ patient year	P value
Stamm et al [7] (randomized placebo controlled trial) 1980	60	Placebo	6 months	2.80	<0.001 (placebo *v* drug treatment)
		TMP-SMZ 40 mg/200 mg at bedtime		0.15	
		Nitrofurantoin 100 mg at bedtime		0.14	
		Trimethoprim 100 mg at bedtime		0	
Melekos et al [8] (randomized open trial) 1997	135	Without prophylaxis	12 months	3.62-3.66	<0.0001
		Ciprofloxacin 125 mg daily		0.031	
		Ciprofloxacin 125 mg postcoitally		0.043	
Nicolle et al [9] (randomized placebo controlled trial) 1989	30	Placebo	12 months	1.6	<0.001
		Norfloxacin 200 mg at bedtime		0	
Brumfitt et al [10] (randomized open trial) 1985	72	Trimethoprim 100 mg at bedtime	12 months	1.00	<0.05
		Nitrofurantoin 100 mg at bedtime		0.17	
Raz et al [11] (randomized open trial) 1991	94	Norfloxacin 200 mg at bedtime	6 months	0.04	0.05
		Nitrofurantoin 50 mg at bedtime		0.60	
Brumfitt et al [12] (randomized open trial) 1991	88	Norfloxacin 200 mg at bedtime	12 months	0.002	not reported
		Nitrofurantoin 100 mg at bedtime		0.003	
Brumfitt et al [13] (randomized open trial) 1995	97	Cefaclor 250 mg at bedtime	12 months	0.006	not reported
		Nitrofurantoin 50 mg at bedtime		0.006	

TMP-SMZ=trimethoprim-sulfamethoxazole

PREVENTING RECURRENCE

QUESTION: Which interventions prevent further recurrence in women experiencing at least two infections per year?

OPTION: CONTINUOUS ANTIBIOTIC PROPHYLAXIS

Evidence from RCTs shows that continuous antibiotic prophylaxis using trimethoprim TMP-SMZ, nitrofurantoin, cefaclor, or a quinolone reduces rates of cystitis in nonpregnant women. There is no good evidence of any difference between continuous regimens, nor between continuous and postcoital regimens.

Benefits

No systematic review. We found seven RCTs comparing different regimens for continuous antibiotic prophylaxis lasting 6 to 12 months in women with high rates of recurrent cystitis (at least two episodes per year) (Table 1).[7-13] Three of the RCTs included a placebo or no-treatment arm.[7-9] All found significantly lower rates of infection with active treatment (nitrofurantoin, trimethoprim, TMP-SMZ, ciprofloxacin, or norfloxacin), but CIs were not given. Versus each other: Five RCTs compared different regimens.[7, 10-13] The comparative evidence for individual drugs is too limited to draw conclusions. Versus postcoital prophylaxis: One RCT compared daily versus postcoital treatment with ciprofloxacin in 135 women.[8] There was no significant difference in rates of infection, but a CI was not given.

Harms

Rates of side effects in these studies ranged from 7-40% for trimethoprim; 0-40% for nitrofurantoin; 5% for cefaclor; 7-21% for norfloxacin; and 13% for ciprofloxacin.[7-9, 11-13] The most common adverse effects for all agents were gastrointestinal symptoms, rash, and yeast vaginitis.

Comment

Many of the studies were not placebo controlled or blinded and had small study populations. Despite the small study

Table 2 *Postcoital regimens for recurrent urinary tract infections: results of RCTs*

Study	Number of participants	Regimen	Duration of prophylaxis	Infections/ patient year	P value
Stapleton et al [14] (randomized placebo-controlled trial) 1990	27	Placebo	6 months	3.6	0.0001
		Postcoital TMP-SMZ 40 mg/20 mg		0.3	
Pfau et al [15] (randomized open trial) 1994	33	Without prophylaxis	14 months	6.13	
		Postcoital prophylaxis with Ofloxacin 100 mg, Norfloxacin 200 mg, Ciprofloxacin 125 mg		0.02	<0.00001
Melekos et al [8] (randomized open trial) 1997	135	Without prophylaxis	12 months	3.62-3.66	
		Ciprofloxacin 125 mg daily		0.031	<0.0001
		Ciprofloxacin 125 mg postcoitally		0.043	
Pfau et al [16] (randomized open trial) 1983	56	Without prophylaxis	12 months	4.6	
		Postcoital prophylaxis with either TMP-SMZ 80 mg/400 mg		0	<0.001
		Nitrofurantoin 50-100 mg		0.1	

TMP-SMZ=trimethoprim-sulfamethoxazole.

sizes, however, differences in infection rates with and without prophylaxis were significant. Adjustments were not made for confounding factors such as frequency of sexual intercourse.

OPTION: POSTCOITAL PROPHYLAXIS

Evidence from RCTs shows that taking nitrofurantoin or a quinolone within two hours after sexual intercourse significantly reduces the rates of infection in women with recurrent cystitis. There is no evidence of any difference between postcoital and continuous antibiotic regimens.

Benefits

No systematic review. We found four RCTs of postcoital antibiotic regimens evaluated over 6 to 14 months in women with high rates of recurrent cystitis (at least two episodes per year) (Table 2).[8, 14-16] Treatment was to be taken within two hours after sexual intercourse. Versus placebo or no treatment: All trials found a significant reduction in rates of infection with active treatment (trimethoprim-sulfamethoxazole, nitrofurantoin or a quinolone). Versus daily prophylaxis: One RCT compared daily versus postcoital treatment with ciprofloxacin in 135 women.[8] There was no significant difference in rates of infection.

Harms

Rates of adverse effects were trimethoprim-sulfamethoxazole 18%; ciprofloxacin 6%; and nitrofurantoin 1%.[8, 14-16] The most common adverse effects for all agents were gastrointestinal symptoms, rash, and yeast vaginitis.

Comment

Only one of the studies was placebo controlled and blinded.[14] Adjustments were not made for confounding factors such as frequency of sexual intercourse.

OPTION: PATIENT-ADMINISTERED TREATMENT

Limited evidence suggests that intermittent patient-administered treatment (taken at the onset of symptoms) is an effective alternative management strategy to continuous antibiotic prophylaxis in women with high rates of infection (at least two per year).

Benefits

No systematic review. We found one RCT using a crossover design in 38 nonpregnant women with two or more culture-documented infections in the previous 12 months.[17] This compared continuous antibiotic prophylaxis with trimethoprim-sulfamethoxazole (40 mg/200 mg) versus a self-administered single dose of trimethoprim-sulfamethoxazole (40 mg/200 mg) to be taken at the onset of symptoms of cystitis. The self-treatment group was given enough tablets for four single treatments. Infection rates were 0.22/year with continuous prophylaxis compared to 2.2/year with self-administered treatment. In the self-treatment group, 85% of infections responded to a single dose.

Harms

There were no significant differences with regard to adverse effects between continuous antibiotic prophylaxis versus self-administered treatment.

Comment

The trial showed that the women were able to diagnose their own infections accurately from symptoms (positive predictive value 92%).[17]

OPTION: LONG-TERM ANTIBIOTIC TREATMENT

Long-term antibiotic prophylaxis (that is, longer than 12 months) has not yet been adequately evaluated in RCTs.

Benefits

No systematic review. No RCTs.

Harms

A cohort study followed 51 nonpregnant women receiving prophylaxis with trimethoprim, trimethoprim-sulfamethoxazole, or nitrofurantoin over 112 patient years. Antibiotic prophylaxis was highly effective in preventing cystitis and pyelonephritis without significant adverse effects, even when used for as long as five years. The development of bacterial resistance from continuous antibiotic prophylaxis was rare; however, the number of trimethoprim-sulfamethoxazole resistant organisms increased during the latter part of the study.[2]

Comment

The RCTs of prophylactic antibiotic regimens, either continuous or postcoital, included only women with a high baseline rate of infection (at least two episodes per year). Although there is some evidence that antibiotic resistance is rare, the decision to initiate long-term prophylaxis should take this possibility into account.

INVESTIGATION OF THE URINARY TRACT

QUESTION: Which women with recurrent infections should undergo investigation for urinary tract abnormalities?

OPTIONS: CYSTOSCOPY, UROGRAPHY, CYSTOGRAPHY, ULTRASONOGRAPHY

Evidence is limited, and no specific subgroups of women who would clearly benefit from investigation have yet been adequately defined.

Benefits

No systematic review. We found no RCTs. Two older, cross-sectional studies[18, 19] and one prospective study[20] examined the yield of routine excretory urography in women with recurrent cystitis. Among the 421 women studied, urography was normal in 88%, showed anatomic variants in about 6%, and was abnormal in about 5%.

None of the abnormalities detected were correctable or thought to be causally related to infection. In two of the studies, cystoscopy also detected no clinically important abnormalities.[19, 20] In a more recent cross-sectional study, 186 women were nonrandomly selected from a larger group of 475 women with recurrent infections because the referring physician suspected an underlying problem.[21] Of these, 21% had an abnormality reported on cystoscopy, excretory urography, ultrasonography, or voiding cystourethrography. Results from this study are difficult to interpret because there was no standard protocol and results were collected retrospectively.

Harms

None of the studies had a sample size large enough to report accurately the incidence of adverse effects in this age group. Excretory urography with iodinated dye can cause anaphylactoid reactions and renal dysfunction. Cystoscopy can cause bleeding and other complications depending upon the type of procedure and anesthesia used. Ultrasonography has no known adverse effects.

Comments

The reported rates of detection of abnormalities are likely to be overestimates because the studies took place in a specialist urology unit.

This paper will be published in *Clinical Evidence* in June 1999. Information about the journal is available on www.evidence.org.

References

1. Hooton TM, Scholes D, Hughes JP, et al. A prospective study of risk factors for symptomatic urinary tract infection in young women. *N Engl J Med* 1996; 335:468-474.
2. Stamm WE, McKevitt M, Roberts PL, White NJ. Natural history of recurrent urinary tract infections in women. *Rev Infect Dis* 1991; 13:77-84.
3. Fihn SD, Latham RH, Roberts P, Running K, Stamm WE. Association between diaphragm use and urinary tract infection. *JAMA* 1985; 254:240-245.
4. Fihn SD, Boyko EJ, Normand EH, et al. Association between use of spermicide-coated condoms and Escherichia coli urinary tract infection in young women. *Am J Epidemiol* 1996; 144:512-520.
5. Mabeck CE. Treatment of uncomplicated urinary tract infection in non-pregnant women. *Postgrad Med J* 1972; 48:69-75.
6. Stamm WE, Counts GW, McKevitt M, Turck M, Holmes KK. Urinary prophylaxis with trimethoprim and trimethoprim-sulfamethoxazole: efficacy, influence on the natural history of recurrent bacteriuria and cost control. Rev Infect Dis 1982; 4:450-455.
7. Stamm WE, Counts GW, Wagner KF, et al. Antimicrobial prophylaxis of recurrent urinary tract infections: a double-blind placebo-controlled trial. *Ann Intern Med* 1980; 92:770-775.
8. Melekos MD, Asbach HW, Gerharz E, Zarakovitis IE, Weingaertner K, Naber KG. Post-intercourse versus daily ciprofloxacin prophylaxis for recurrent urinary tract infections in premenopausal women. *J Urol* 1997; 157:935-939.
9. Nicolle LE, Harding GKM, Thompson M, Kennedy J, Urias B, Ronald AR. Prospective, randomized, placebo-controlled trial of norfloxacin for the prophylaxis of recurrent urinary tract infection in women. *Antimicrob Agents Chemother* 1989; 33:1032-1035.
10. Brumfitt W, Smith GW, Hamilton-Miller JMT, Gargan RA. A clinical comparison between macrodantin and trimethoprim for prophylaxis in women with recurrent urinary infection. *J Antimicrob Chemother* 1985; 16:111-120.
11. Raz R, Boger S. Long-term prophylaxis with norfloxacin versus nitrofurantoin in women with recurrent urinary tract infection. *Antimicrob Agents Chemother* 1991; 35:1241-1242.
12. Brumfitt W, Hamilton-Miller JMT, Smith GW, Al-Wali W. Comparative trial of norfloxacin and macrocrystalline nitrofurantoin (Macrodantin) in the prophylaxis of recurrent urinary tract infection in women. *Q J Med* 1991; 81:811-820.
13. Brumfitt W, Hamilton-Miller JMT. A comparative trial of low-dose cefaclor and macrocrystalline nitrofurantoin in the prevention of recurrent urinary tract infection. *Infection* 1995; 23:98-102.
14. Stapleton A, Latham RH, Johnson C, Stamm WE. Postcoital antimicrobial prophylaxis for recurrent urinary tract infection: a randomized, double-blind, placebo-controlled trial. *JAMA* 1990; 264:703-706.
15. Pfau A, Sacks TG. Effective postcoital quinolone prophylaxis of recurrent urinary tract infection in women. *J Urol* 1994; 152:136-138.
16. Pfau A, Sacks T, Englestein D. Recurrent urinary tract infections in premenopausal women: prophylaxis based on an understanding of the pathogenesis. *J Urol* 1983; 129:1153-1156.
17. Wong ES, McKevitt M, Running K, Counts GW, Turck M, Stamm WE. Management of recurrent urinary tract infections with patient-administered single-dose therapy. *Ann Intern Med* 1985; 102:302-307.
18. Fair WR, McClennan BL, Jost RG. Are excretory urograms necessary in evaluating women with urinary tract infection? *J Urol* 1979; 121:313-315.
19. Engle G, Schaeffer AJ, Grayhack JT, Wendel EF. The role of excretory urography and cystoscopy in the evaluation and management of women with recurrent urinary tract infection. *J Urol* 1980; 123:190-191.
20. Fowler JE Jr, Pulaski ET. Excretory urography, cystography, and cystoscopy in the evaluation of women with urinary tract infection: a prospective study. *N Engl J Med* 1981; 304:462-465.
21. Nickel JC, Wilson, J, Morales A, Heaton J. Value of urologic investigation in a targeted group of women with recurrent urinary tract infections. *Can J Surg* 1991; 34:591-594.

ANY QUESTIONS?

Do you have a clinical question you'd like to see answered? If so, here's your chance to get a curbside consult from our expert team, which includes many of the top clinicians in the West.

ANY ANSWERS?

Maybe you have strong views about something you read in this issue—something we got wrong perhaps? Or do you have further clinical experience you'd like to share? Perhaps you have suggestions for new topics you'd like to see addressed from an evidence-based perspective. Every clinical practice is different and we want to know what you've learned that might benefit others. Similarly, what can your colleague provide that can improve your practice?

Whatever questions, comments or other contributions you have, we'd like to receive them. We realize that it's experience like yours that will make the journal come alive. Please send in your questions/ideas/comments by e-mail or fax to:
Catherine Nancarrow, Editorial Manager, *WJM Western Journal of Medicine;* wjmsf@pacbell.net; fax 415-882-3379.

MEDICINE CABINET

Treatment advances in rheumatoid arthritis

Edgar R Arriola
Nancy P Lee
UCLA Medical Center
Department of
Pharmaceutical Services
10833 Le Conte Avenue
CHS 16-131
Los Angeles, CA 90095

Correspondence to:
Dr Arriola
earriola@mednet.ucla.edu

Rheumatoid arthritis (RA) is a chronic, often debilitating autoimmune disorder characterized by persistent synovial inflammation that leads to cartilage and bone destruction. RA afflicts over 2 million Americans and contributes to substantial morbidity and increased mortality. It is estimated that one third to one half of patients suffering from RA may have moderate to severe disease. Unfortunately, there is currently no cure for RA. Management strategies are primarily focused on reducing pain and inflammation, preserving range of motion, and slowing disease progression.

In the past, drugs often had serious side effects and limited efficacy. Over the past year, several new options have emerged for the management of RA. These products include new formulations/combinations of existing products (e.g., diclofenac/misoprostol, Arthrotec®), additional refinements to existing pharmacologic classes of medications, and new approaches that target the underlying processes that perpetuate RA. This article will highlight some of these advancements.

CELECOXIB (CELEBREX™)

Celecoxib (Celebrex™, G.D. Searle & Co, Pfizer, Inc.) was approved by the FDA in December 1998 for the relief of signs and symptoms of osteoarthritis (OA) and RA. It is the first of several non-steroidal anti-inflammatory drugs (NSAIDs) referred to as "selective" COX-2 inhibitors.

According to adverse drug reaction reports obtained under the Freedom of Information Act, celecoxib has been associated with 10 deaths and 11 cases of gastrointestinal hemorrhages since its introduction in the United States.[1] It is important, however, to emphasize that these cases have not been fully analyzed and causality has not been established.

As with many new drugs, the full safety profile of celecoxib may not be realized until it has been exposed to widespread use and additional trials are completed. At this time, the FDA has not issued any additional warnings.

Pharmacology

COX (cyclooxygenase) is the first enzyme in the prostaglandin synthesis pathway. It exists in two isoforms, COX-1 and COX-2, with COX-1 being expressed constitutively in most tissues. COX-2 exists in lower levels and is inducible by various stimuli including cytokines, mitogens, and endotoxins.[2] It is found in the brain and kidneys. The current hypothesis is that COX-2 is primarily responsible for prostaglandin synthesis in the inflammatory process whereas COX-1 is involved in prostaglandin synthesis for normal homeostasis.[3] Most NSAIDs currently available inhibit both COX-1 and COX-2. Celecoxib has a 375-fold greater affinity for COX-24.[4]

Clinical trials

Published clinical data are limited to short-term phase II trials. The results of four phase II trials were recently reported by Simon et al.[5] In a 2-week phase II OA trial comparing 40 mg, 100 mg, or 200 mg celecoxib twice daily versus placebo, celecoxib was statistically superior to placebo as evaluated by both patients and physicians. Similar results versus placebo were obtained in a 4-week RA trial comparing 40 mg, 200 mg, or 400 mg celecoxib twice daily; however, the 40 mg twice daily group failed to reach statistical significance after the first week. The remaining phase II trials consisted of an endoscopic assessment of gastrointestinal tolerance and an assessment of platelet effects. In the endoscopy trial, celecoxib and placebo produced no gastric ulcers (defined as any lesion of any size with unequivocal depth) compared to 19% of naproxen treated patients following 1 week of therapy. No meaningful effects on platelet aggregation or thromboxane B2 levels were observed following 5 days of therapy.

A summary of unpublished clinical trials is available from the manufacturers product package insert.[6] In RA trials of up to 24 weeks duration, celecoxib 100 mg or 200 mg twice daily was superior to placebo and comparable to naproxen 500 mg twice daily. In some patients, the 200 mg twice daily dose provided additional benefit; however, no additional benefit was gained with doses of 400 mg twice daily.

Pharmacokinetics

Following oral administration, peak levels are achieved at approximately 3 hours. Celecoxib may be administered without regard to meals. Celecoxib has an effective half-life of 11 hours and is eliminated by metabolism primarily via cytochrome P450 2C9. Fluconazole and other inhibitors of 2C9 may increase celecoxib levels. Celecoxib may increase lithium levels in patients on lithium therapy. Preliminary studies in normal subjects receiving warfarin did not reveal an alteration in anticoagulant effect.

Adverse events

Adverse events reported in these trials consisted of headache, diarrhea, rhinitis, nausea, sinusitis, dyspepsia, and abdominal pain. The incidence of these reactions was similar to those observed in the placebo group. Laboratory abnormalities observed in these short-term trials included isolated elevations in biliary and liver function tests.

Administration

The recommended dose of celecoxib for OA is 200 mg daily either as a single dose or in two divided doses. For RA, the recommended dose is 100 mg to 200 mg twice

daily. It is available in 100-mg and 200-mg capsules and has been priced competitively with other proprietary NSAIDs (see Table 1).

Celecoxib appears to be effective in treating OA and RA. Whether COX-2 selective NSAIDs will produce fewer episodes of serious gastrointestinal bleeding awaits further clinical trials. The FDA has taken a cautious approach. Their approval letter states, "that any advertising and/or promotional activity of this product will be considered false and/or misleading...if it presents suggestions or representations that COX-2 selectivity confers on the product any claims of safety beyond what has been demonstrated in clinical studies and presented in the approved labeling."

LEFLUNOMIDE (ARAVA™)

Leflunomide (Arava™, Hoechst Marion Roussel) is a new immunomodulatory agent approved for the treatment of active RA. It is the first oral agent to receive labeling for use in reducing signs and symptoms of RA and in retarding structural damage as evidenced by x-ray erosion and joint space narrowing. Leflunomide is structurally unrelated to other available disease-modifying anti-rheumatic drugs (DMARDs).

Pharmacology

Although the etiology of RA has not yet been fully elucidated, the role of T cells in the pathogenesis of RA has been implicated.[7] Leflunomide is thought to disrupt T-cell proliferation through the inhibition of dihydroorotate dehydrogenase, an enzyme involved in the de novo synthesis of pyridmidine.[8]

Clinical Trials

In the US/Canadian trial (unpublished data), 482 patients with active RA were randomized to treatment with leflunomide (20 mg/day), methotrexate (7.5 mg titrating to 15 mg/week), or placebo for 52 weeks.[9] Leflunomide and methotrexate were both statistically superior to placebo in reducing the signs and symptoms of RA as assessed by the primary efficacy measure, the American College of Rheumatology (ACR) 20 responder rate at study endpoint. ACR20 responder rates at endpoint were 41% for leflunomide, 35% for methotrexate, and 19% for placebo. No difference was detected between the two active groups. Mean changes in X-ray Sharp Score, a measure of structural damage resulting from disease progression, were +0.5 for leflunomide, +0.9 for methotrexate, and +2.2 for placebo.

In a supportive, non-placebo-controlled European trial (unpublished data), 999 patients with active RA were randomized to treatment with leflunomide (20 mg/day) and methotrexate (7.5 mg titrating to 15 mg/week).[9,10] At 52 weeks, both treatments produced clinically significant improvements over placebo. No difference in Sharp Score was detected.

The only published phase III study to date is a short-term placebo-controlled European trial comparing leflunomide (20 mg qd) with sulfasalazine (2 g qd).[11] Both agents were equally efficacious in reducing joint counts and improving global assessments. Radiographic assessment of disease progression was similar between the two active groups.

Overall, treatment effect of leflunomide was observed by 1 month, stabilized by 3 to 6 months, and maintained throughout course of treatment.

Pharmacokinetics

Leflunomide is a prodrug that is rapidly converted to its main active metabolite, A77 1726. This active metabolite is further metabolized and undergoes both renal and biliary excretion. The prolonged half-life of leflunomide (approximately

Table 1 *Relative cost comparison of selected agents*

Agent	Usual Dose	Estimated Cost / month (based on AWP)
Celecoxib (Celebrex™)	OA: 200 mg po qd RA: 100-200 mg po bid	$72.60 to $145.20
Naproxen (Naprosyn®) generics available	500 mg po bid	$80.40
Ibuprofen (Motrin®, Advil®) generics available	800 mg po tid	$25.20
Diclofenac/misoprostol (Arthrotec®)	OA: 50 mg/200 mg po tid	$126.00 to $168.00
	RA: 50/200 mg po tid-qid	
Leflunomide (Arava™)	20 mg po qd	$244.80
Methotrexate (Rheumatrex®) generics available	7.5 to 15 mg po weekly	$42.00 to $84.00
Etanercept (Enbrel™)	25 mg sc twice weekly	$1,100.00

2 weeks) is attributed to its high protein binding and enterohepatic recirculation.[12] Therefore, a loading dose is necessary to rapidly attain therapeutic plasma levels.

Administration of cholestyramine and activated charcoal results in rapid reduction in plasma concentration of the active metabolite (these agents may be used therapeutically to accelerate drug removal). The active metabolite of leflunomide is also noted to inhibit cytochrome P450 2C9. Plasma levels of certain NSAIDs and tolbutamide may be increased when given with leflunomide. Concomitant administration with rifampin has been shown to increase plasma levels of the active metabolite by up to 40%.

Adverse reactions

Adverse reactions observed with leflunomide therapy (from all RA trials) include diarrhea (17%), abnormal liver enzymes (5%), alopecia (10%), and rash (10%). In comparative trials, treatment-related adverse events occurred in 74-75.8% of leflunomide-treated and in 63.2-72% of methotrexate-treated patients.

Elevations in liver enzymes occurred in a significant number of patients during clinical trials although most elevations were mild and transient. Marked elevations (>3 × ULN) were rare and resolved with dose reduction or treatment discontinuation. A baseline liver function test be performed and followed monthly at the onset of therapy, then if stable, at intervals determined by the individual clinical situation. Preliminary results from a small study found the risk of hepatotoxicity to be significantly increased when dual therapy with methotrexate was utilized.[13]

Leflunomide is classified under Pregnancy Category X. Women who are or may become pregnant should avoid its use (the need for reliable contraception should be enforced for patients of childbearing age). An accelerated drug elimination procedure (cholestyramine 8 g tid for 11 days) is recommended for patients who want to become pregnant after discontinuation of leflunomide to minimize exposure to the fetus. Men wishing to father a child should also discontinue leflunomide therapy and undergo an accelerated drug elimination procedure.

Administration

Therapy should be initiated with a loading dose of 100 mg daily for 3 days. The recommended maintenance dose is 20 mg daily. While treated with leflunomide, patients may be maintained on aspirin, NSAIDs, and/or low dose corticosteroids.

Leflunomide appears to be an effective agent for the management of active of RA. Available data show comparable efficacy with methotrexate and sulfasalazine; however, it remains to be seen whether or not leflunomide demonstrates a clear clinical advantage over methotrexate, the current first-line DMARD for active RA. Additional studies are required to establish long-term clinical efficacy and safety.

ETANERCEPT (ENBREL™)

The FDA also recently approved the first biotechnology product, etanercept (Enbrel™; Immunex Corp.), for reduction in signs and symptoms of moderately to severely active RA in patients who are refractory to treatment with one or more DMARDs. It can also be used with methotrexate in patients who do not respond adequately to methotrexate alone.

Pharmacology

Etanercept is a dimeric soluble form of the TNF receptor that can bind two TNF molecules. Etanercept inhibits the binding of both TNF alpha and TNF beta to the cell-surface TNF receptor, thus inhibiting activity.[14] While the causes of RA are not fully understood, it is felt that proinflammatory cytokines such as TNF may be significant factors in its pathogenesis.

Clinical trials

Moreland et al., conducted a multicenter, randomized, double-blind trial of etanercept in 180 patients with refractory RA who had not responded to one or more of the following DMARDs: hydroxychloroquine, gold, methotrexate, penicillamine, sulfasalazine, or azathioprine.[15] A significant improvement in all measures of disease activity was achieved in patients randomized to etanercept. A clear dose-response relation in swollen/tender joint reduction at 3 months was observed, with patients receiving the highest dose level of etanercept (16 mg/m^2) having the greatest improvement (61% vs. 25%, etanercept vs. placebo, P>0.001). Seventy-five percent of patients in the highest dose group had a ≥ 20% improvement in symptoms at 3 months compared to 14% of placebo patients (P<0.001). Etanercept was also associated with reductions in pain and duration of morning stiffness, physician's and patient's global assessment, improved quality of life, and reduced ESR and C-reactive protein.

Etanercept was also evaluated as an add-on treatment in a short-term study.[16] Patients with persistent RA, despite therapy with methotrexate for at least 6 months, were randomized to treatment with etanercept-plus-methotrexate or placebo-plus-methotrexate. At 24 weeks, the combination regimen achieved significantly greater efficacy for all endpoints according to ACR response criteria. The ACR 20 responder rate was 71% for the etanercept-plus-methotrexate group and 27% for the placebo-plus-methotrexate group (P<0.001). The

response seen with this combination regimen was rapid and sustained. Injection site reactions were the only events that occurred significantly more often in the combination group; potentiation of toxicities was not observed.

Pharmacokinetics

With single subcutaneous injections, a median half-life of 115 hours (range 98 to 300 hours) was observed. Upon chronic administration, the median steady-state serum concentration was 3.0 µg/L (range 1.7 to 5.6 µg/L). These pharmacokinetic parameters did not vary with age or gender.

Adverse events

Etanercept was generally well tolerated with no dose-limiting toxicity observed. The most common adverse effects associated with etanercept administration were injection site reactions which generally did not require discontinuation. Other adverse events reported in clinical trials included mild upper respiratory tract symptoms such as cough, rhinitis, sinusitis, URI, and pharyngitis. Non-neutralizing antibodies were detected in about 16% of patients but did not correlate with clinical outcome nor adverse events. The long-term immunogenicity of etanercept remains unknown.

Administration

Etanercept is available in cartons containing four-dose trays consisting of one 25-mg single-dose vial etanercept, diluent, syringe, and alcohol wipes. The recommended adult dose is 25 mg subcutaneously given twice weekly. The cost per month of therapy is listed in Table 1.

A similar agent, infliximab (Remicade™), is also being studied in rheumatoid arthritis and may obtain FDA approval for this indication.[17] It was recently FDA-approved for the treatment of Crohn's disease. Infliximab differs from etanercept in that it is a monoclonal antibody and is administered intravenously. A potential advantage of infliximab may include less frequent intravenous administration (every 4-12 weeks), while a disadvantage may include the potential development of antichimeric antibodies and decreased efficacy with repeated doses. It is unknown what the approved dose or final cost will be for this indication.

Etanercept is the first anti-TNF product approved for the treatment of RA in patients with moderate to severe disease who have failed to respond to one or more DMARDs. It has demonstrated efficacy in decreasing symptoms of RA; however, its effect on disease progression and potential long-term effects of anti-TNF drugs has not been determined. Discontinuation of therapy results in reappearance of symptoms within one month. Similar agents may gain FDA approval in the near future. While the exact role of etanercept or other TNF inhibitors remains to be determined, they do offer a treatment alternative for patients who have failed to respond to other treatment modalities.

References

1. Sharpe R. Several deaths show a link to Celebrex. *Wall Street Journal* (Tuesday, April 20, 1999): B6, C1.
2. Pincus T, Callahan LF, Sale WG, et al. Severe functional declines, work disability, and increased mortality in seventy-five rheumatoid arthritis patients studied over nine years. *Arthritis Rheum* 1984; 27:864-72.
3. Mitchell JA, Akarasereenont P, Thiemermann C, Flower RJ, Vane JR. Selectivity of nonsteroidal antiinflammatory drugs as inhibitors of constitutive and inducible cyclooxygenase. *Proc Natl Acad Sci* 1994; 90:11693-97.
4. Seibert K, Zhang Y, Leahy K, et al. Pharmacological and biochemical demonstration of the role of cyclooxygenase 2 in inflammation and pain. *Proc Natl Acad Sci* 1994; (91):12013-17.
5. Simon LS, Lanza FL, Lipsky PE, et al. Preliminary study of the safety and efficacy of sc-58635, a novel cyclooxygenase 2 inhibitor. *Arthritis Rheum* 1998; (41):1591-1602.
6. Product monograph, CelebrexTM. G.D. Searle & Co. Skokie, IL, December 1998.
7. Breedveld FC. New insights in the pathogenesis of rheumatoid arthritis. *J Rheumatol* 1998; 25:3-7.
8. Davis JP, Cain GA. The immunosuppressive metabolite of leflunomide is a potent inhibitor of human dihyoorotate dehydrogenase. *Biochemistry* 1996; 35:1270-3.
9. Product monograph, Arava™. Hoechst Marion Roussel. Kansas City, MO, September 1998.
10. Personal Communication, C Howe, RPh, Manager, Medical Informatics, Hoechst Marion Roussel, Kansas City, MO. February 19, 1999.
11. Smolen JS, Kalden JR, Scott DL, et al. Efficacy and safety of leflunomide compared with placebo and sulphasalazine in active rheumatoid arthritis: a double-blind, randomised, multicentre trial. *Lancet* 1999; 353:259-66.
11. Fox, RI. Mechanism of action of leflunomide in rheumatoid arthritis. *J Rheumatol* 1998; 25: 20-26.
12. Weinblatt ME, Kremer JM, Coblyn JS, et al. Leflunomide plus methotrexate in refractory rheumatoid arthritis. *Am Coll Rheumatology* 1997; 40(9):974 [Abstract].
13. Product monograph, EnbrelJ. Immunex Corp. Seattle, WA, November 1998.
14. Moreland LW, Baumgartner SW, Schiff MH, et al. Treatment of rheumatoid arthritis with a recombinant human tumor necrosis receptor (p75)-Fc fusion protein. *NEJM* 1997; 337:141-7.
15. Weinblatt, ME, Kremer JM, Bankhurst AD, et al. A trial of etanercept, a recombinant tumor necrosis factor receptor:Fc fusion protein, in patients with rheumatoid arthritis receiving methotrexate. *NEJM* 1999; 340:253-9.
16. Maini RN, Breedveld FC, Kalden JR, et al. Therapeutic efficacy of multiple intravenous infusions of anti-tumor necrosis factor alpha monoclonal antibody combined with low-dose weekly methotrexate in rheumatoid arthritis. *Arthritis Rheum* 1998; 41:1552-63.

capsule

Chest pain can be due to an over active esophagus The esophagus is often blamed for non cardiac chest pain and investigators from Virginia report that abnormally long contractions of the wall could be the cause of it (*Gastroenterology* 1999; 116;29-37). They used continuous endoluminal ultrasonography to record what happened before, during and after chest pains in 20 volunteers. Contractions lasting over one minute usually preceded the pain.

Is bungee jumping safe?

Bungee jumping is safer than it looks. *Courtesy of J. Shipley.*

In bungee jumping, participants leap off a raised launch site, most commonly a tower, crane, or hot air balloon, and fall freely until stopped by a bungee cord made up of multiple strands of tightly bound rubber. Over the past decade this activity has become increasingly popular. Several deaths and serious injuries related to bungee jumping have been reported by the press. In 1994 we surveyed jumpers at a professionally run bungee jumping site, where participants jumped off a fixed 130 foot (39.4 meter) structure.[1] We found that almost half of the jumpers (42%) had a medical complaint after jumping. These included six reports of headaches, seven episodes of blurred vision, 21 episodes of dizziness, one episode of transient numbness of the leg, and 21 complaints of muscular pain (two in the neck, three in the back, one in the chest, 12 in the ankle, and three in the abdomen). However, except for a person who changed his mind midlaunch and suffered multiple lacerations to his arms and legs as he tried to grab the platform, these complaints were minor and had resolved within one week of jumping. Thus we conclude that a single bungee jump under professional supervision is relatively safe.

References
1. Young C, Raasch W, Boymon M. After the fall: symptoms in bungee jumpers. *Physician Sports Med* 1998; 26:75-78.

Craig Young
Musculoskeletal and Arthritis Center,
Medical College of Wisconsin Clinics at Froedtert East,
9200 Wisconsin Avenue,
Milwaukee, WI 53226-0099

What advice can I give my patients with lymphedema?

Lymphedema is a condition in which protein rich fluid accumulates in the extravascular, interstitial spaces. In clinical practice, most lymphedema is iatrogenic secondary to the disruption of lymphatic channels during the treatment of cancers using surgery, radiation, or both.

Cancer patients find lymphedema physical and psychologically debilitating. Initially symptoms are mild consisting of swelling which usually responds to limb elevation. As time passes symptoms often worsen with the development of pain, recurrent cellulitis and loss of function. The limb looks unsightly and is a constant reminder of cancer.

My first step when a patient presents with lymphedema is to make sure there are no other causes such as venous thrombosis or recurrent cancer. Once other diagnoses are excluded I evaluate and quantify the extent of edema in the tissues by observation, palpation and measurement of both arms to compare them to each other. The measurement is done at several points in the arms including 10cm above and below the olecranon and 5cm above the wrist. A difference of 1 cm between the dominant and the non dominant arm is usually normal. I consider a difference of 2cm or more denotes lymphedema.

Specially trained lymphedema therapists can provide a more complete measurement of the actual volume of fluid in the tissues. Therapists are also trained to provide combined or complex physical decongestive therapy which consists of gentle massage to mobilize fluid from the affected arm and to help open new lymphatic channels that can carry the fluid out of the affected limb. They also bandage the affected limb with gradual compression and when the edema has been sufficiently reduced they will measure the patients for special compression garments. The largest reduction in lymphedema volume as well as the best symptomatic relief is obtained for those patients who do not have a large quantity of fluid in the tissues. As the lymphedema continues and the tissues fibrose, it becomes more difficult to get good results, although symptoms can be relieved even with small changes in the volume of edema. Lastly, lymphedema therapists can educate patients about the condition and self management. Techniques I find most useful are:

- Daily self massaging of affected limb
- Daily bandaging of the limb and eventually daily use of compression garment
- Meticulous attention to hygiene of the arm with daily inspection and use of water soluble moisturizing creams
- Decompressive exercises if the patient is not very active or in the normally active patient, vigorous use of the affected arm and elevation when at rest

Lymphedema makes limbs more susceptible to infection which is often difficult to treat and leads to further tissue damage and lymph stasis. Patients should take great care to avoid any trauma (e.g. shaving, venipuncture, or acupuncture). I advise people with lymphedema to use protective gloves when performing housework and gardening. If wounds do occur I encourage prompt cleansing and a call to the physician for possible early antibiotics. Other advise I give is to avoid having blood pressure measurements taken in the affected arm, avoid wearing tight-fitting jewelry (rings, bracelets etc.) and carrying heavy loads, and keeping the extremity still and dependent for prolonged periods. Elastic bandages or compression garments are helpful when flying or driving for prolonged periods.

Despite all these cautions I encourage my patients to lead active lives which remembering that they do have a chronic condition and common sense can keep them from developing further problems.

Sylvia M Ramos
717 Encino Place N.E.,
Suite#14,
Albuquerque NM 87102

Why do people yawn?

Remarkably little interest has been paid to yawning in research, even though it is an everyday phenomenon. Observation suggests that yawning is a semivoluntary act associated with boredom and fatigue, and it seems to be contagious in a room of similarly affected people. But why do fetuses yawn, and what is the physiological purpose of yawning?

The yawning reflex can be triggered by drugs or by psychological, hormonal, or neurological stimuli. Yawning occurs at as early as 15 weeks in an embryo, and newborn babies usually yawn shortly after they take their first breath. All vertebrates yawn, and yawning persists in people who are in a vegetative state. Such universality suggests that yawning has a defensive or protective function.

The reflex arc is thought to be in the reticular system of the brain stem, and it involves the respiratory neurons in the medulla; the motor nuclei of the 5th, 7th, 10th, and 12th cranial nerves; the phrenic nerves; and the motor supply to the intercostal muscles. Neurological lesions tell us much about the functioning of the brain; they confirm that the yawning center is part of the reticular system because people with pontine lesions who cannot open their mouths at will are able to yawn in response to appropriate stimuli. The reticular complex is closely connected to cortical areas, the subcortical limbic center, and the hypothalamus, which explains why boredom, fatigue, and the act of observing others yawning can provoke the reflex through the prefrontal associative area.

Endorphins play an important role in yawning. Apomorphine, a dopaminergic receptor agonist, so reliably stimulates yawning that apomorphine-induced yawning is used as a test of the integrity of dopaminergic function in patients with neurological disorders such as Parkinson's disease. Increased serotoninergic activity also induces yawning, acting in concert with cholinergic influences. This increase in cholinergic activity acts through negative feedback to decrease serotonin and noradrenaline concentrations and thereby reducing the tendency to sleep. Yawning, therefore, has an alerting, antisleep effect, which is probably enhanced by the generalized stretching movements that often accompany a yawn.

Yawning can be induced in those who are not bored just by thinking about it.

Studies have shown that yawning predicts a subsequently increased level of activity. However, the rate of yawning is not dependent on the amount of previous sleep or the time of waking or retiring to bed. More yawning occurs during the week than at weekends.

Yawning is a feature of some pathological states. The frequency of yawning is reduced in Parkinson's disease, and it may occur more often in epilepsy and in states of opiate withdrawal. In patients who have had a stroke affecting the pyramidal tract in the internal capsule region, stretching movements of the hemiplegic arm may occur during spontaneous or apomorphine induced yawning. Yawning induced cerebral ischemia (in the form of a transient ischemic attack) in a patient who had undergone bypass surgery when the accompanying vigorous movement of the jaw muscle occluded the temporal and middle cerebral arteries. In comatose patients the onset of yawning predicts the imminent return of wakefulness.

Yawning has been associated with a minor degree of hypoxia in patients with cerebrovascular disease. This has led to the idea that the function of yawning is to generate a large inspiration to overcome borderline hypoxia and hypercapnia. If this were true, the incidence of yawning would be reduced by breathing high concentrations of oxygen and would be increased by raising the partial pressure of carbon dioxide. Studies have shown that this does not occur, and yawning is not a major clinical feature in patients with acute or chronic ventilatory failure.

From a behavioral point of view, when yawning seems to be contagious, similar external stimuli (or the lack of stimuli) are likely to affect all of those present. However, yawning can be induced in those who are not bored just by thinking about it. These socioenvironmental influences indicate a communicative function, and the reflex may act as a nonverbal cue in generating social cohesion.

We can probably conclude that yawning has an important role as an arousal mechanism to maintain alertness and defend against the onset of sleep. It can be affected by a range of behavioral influences, but much still needs to be learned about this everyday activity.

This article was originally published in *Student BMJ* 1998; 6:191.

Anita K Simonds
Department of Respiratory Medicine,
Royal Brompton Hospital,
London SW3 6NP

TOOLBOX

Taking a sexual history

John Tomlinson, Clay Farm, East Worldham, Hampshire, GU34 3AD, UK
Etan C Milgrom, Department of Family Medicine, University of California, Los Angeles, CA
Correspondence to: Dr Milgrom emilgrom@fammed.medsch.ucla.edu.

Many doctors feel uncomfortable about their ability to take an appropriate history from a patient with a sexual problem. In part, the discomfort lies in the doctor's feelings of embarrassment and the patients ambivalence about bring up the topic. Patients may feel ashamed or even humiliated at having to ask for help with a sexual problem that they consider private and that they should be able to cope with themselves. This is particularly so with men, especially young men, who have to admit to erectile dysfunction and therefore, as they see it, the loss of their masculinity. Some physicians have found that they can avoid this initial difficulty by giving patients a waiting room preconsultation written questionnaire. Many patients like this but some dislike its anonymity and apparent coldness.

As with other history taking, the doctor must carefully choose words, avoid close-ended questions, be nonjudgmental, avoid labels with hidden meaning and carefully observe body language.

Interview technique

Above all, there must be sufficient time allowed, and 45-60 minutes is an ideal that is unfortunately not often possible to achieve, especially as managed care invades our health care system. A patient's ability to bring up a sexual problem may be tentative and hidden by euphemisms, with statements like "I think I need a check up" or "by the way, I have a [discharge, itch, soreness] down below." These comments may well be slipped into a visit about some other medical. Various interview techniques can be used to help patients feel more comfortable during the interview. These include the manner of greeting a patient, seeing that the patient is seated comfortably, and ensuring privacy (especially in a clinic setting). Very early in the discussion, the patient must be assured of confidentiality, particularly with regard to clinic and hospital staff. If the seat is placed at the side of the desk, there is more opportunity to observe the patient's body language, as well as this being a more friendly arrangement.

Patients' body language, such as defensively crossing arms, can sometimes give hints as to their state of mind.

We find that useful observations on patients' body language include:

- Their use of their hands and arms such as uneasily fiddling with a ring, defensively crossing arms, or protectively holding a bag or briefcase on a lap.
- Pectoral flush, which creeps over the upper chest and neck (in some younger men as well as women) and suggests unease despite an outward appearance of calm.
- The body's position in the chair is a depressed slump, or tautly sitting upright, or the relaxed sprawl.
- Postural echo, when doctor and patient sit in mirror images of each other's position adopted when there is harmony and empathy between the doctor and patient.

When people talk about embarrassing subjects, they are often vague and in direct. The clinician should try to clarify their meaning. Words such as "impotence," for example, can mean different things to different men (and their partners), including failure to get an erection, failure to maintain an erection, and premature ejaculation. Similarly, a phrase such as "I'm sore down below" can mean anything from pruritus ani to some anatomical problem such as a prolapse or genital warts. Careful and tactful elucidation is needed, and vagueness must be clarified. The questioner has to be particularly sharp in picking up what the patient is trying to say and be relaxed and unfazed by the subject matter. Physicians need to be careful not to overstate their concern.

Factors to be noted during the interview include:

- The patient's sexual preference for men, women or both
- Cohabitational status (married, living with partner, etc.)
- Approximation of previous life time sexual partners; approximation of partners in past six months
- How long has patient been with the current partner?
- Does the patient have children? Who do they live with?
- Is there stress between the patient and their sexual partner or in the family?
- What types of sexual behaviors does the patient engage in? How often? Are these activities mutual enjoyable?
- If the patient is a female, it is important to ask about menstrual history and regularity of cycles
- Use of birth control
- History of sexually transmitted diseases
- For both men and women it is important to ask about a history of being sexually abused (including rape, child abuse, domestic violence)
- Use of prescribed medications or recreational drugs

Choice of terminology

One difficulty that bothers many doctors is whether to use vernacular terms in discussions because of their emotional charge, or whether to use only medical terms. We believe it best to avoid a hard and fast rule but to tailor the terminology to the patient. Patients too, because of embarrassment about using colloquialisms and fear of causing offense, may try to express their problem

with inaccurate medical terminology. Both can cause problems in getting an accurate history. Some younger patients, especially women patients, may not know the meaning of "orgasm" but will understand "come." While fellatio and cunnilingus are not words in general use, the use of their street equivalent would allow for a more relaxed and empathic discussion. Certainly, "oral sex" is more acceptable to men and women of all ages. Usually, the line is very fine and is often related to age and gender.

A 16-year-old was struggling to find medical words to explain his anxieties about masturbation and ejaculation. When the doctor tried to help him out by using colloquial terms the boy looked startled and then grinned and said, "I didn't know doctors knew those words." The rest of the consultation was much more relaxed and informative.

Communication

The way open and closed questions are used in proper history taking are crucial, but take on an even greater importance when taking a sexual history. A closed question demands a specific reply, such as "Yes" or "No". Characteristic closed ended questions include: "Have you had this problem before? Does it hurt when you pass water? Did you practice safe sex?"

Starting with an open question "How can I help you?" and continuing with open ended questions such as "what do you think caused the difficulty?" gives patients more opportunity to expand on their concerns. Many younger doctors are worried that a garrulous person might get out of hand, but remaining in control is a skill a good interviewer learns quickly. Judgmental questions, "You didn't have sex with a prostitute did you?" "You don't allow him to have anal intercourse do you?" should be avoided like a sexually transmitted disease.

Silence is a powerful tool in taking a good history. Many doctors find it extremely difficult to endure a moment of silence. In fact, most doctors can not endure more than 5 seconds of not talking themselves. Silence can be an extremely useful tool if used properly. The patient often uses this time to order his or her thoughts. Valuable details may be lost if those thoughts are cut interrupted by an inappropriate statement from the doctor. A rule of thumb is to wait for an answer; it will come.

Another useful tool is to use the "echo" or verbal repetition to elicit information. Repetition of the last word or phrase, especially if it is one which is full of emotionally loaded, is a powerful technique and can elicit much information, although it may seem artificial at first.

As an example:

"Doctor, I think I need a check up"
"Yes, of course. It's been a while since the last one. Let me start with your blood pressure…."

Compare this with

"Doctor, I think I need a check up"
"Check up?"
"Yes, I'm not performing as well as I used to"
"Performing?"
"Yes, well, you know, I think I'm impotent. My wife is very good about it and doesn't complain, but I feel so guilty and ashamed"
"Ashamed?"
"I feel terrible. I don't feel a man any more, especially as we used to have such a good sex life…."

Although a joint interview is always much more valuable, patients often prefer to discuss things alone in the first instance. A warm invitation for the partner, coupled with the observation that a sexual problem is not the patient's problem alone, can put the patient's anxieties into perspective.

To be complete, the history (see box) must include several factors.

Social history

A detailed social history helps put the patient's sexual difficulties into context. Taking a social and medical history before exploring the problem allows the patient time to relax while talking about familiar things such as home, children and work and enables the doctor to put the problems into perspective. Even if the doctor knows the patient well, a review of the social history will update the patient's chart and new information may be uncovered that could be relevant to the current sexual problem.

Questions to be asked in sexual history

- What is the problem as the patient sees it?
- How long has the problem been present?
- Is the problem related to the time, place, or partner?
- Is there a loss of sex drive or dislike of sexual contact?
- Are there problems in the relationship?
- What are the stress factors as seen by the patient and by the partner?
- Is there other anxiety, guilt, or anger not expressed?
- Are there physical problems such as pain felt by either partner?

Medical history

It used to be thought that all sexual problems, especially erectile dysfunction, were psychogenic in origin. General opinion has shifted to accepting that a large proportion have a physical basis, though, not surprisingly, often with a psychogenic overlay. It is therefore important to take a detailed medical history, particularly bearing in mind those illnesses that may affect sexual performance. Diabetes can eventually cause impotence in up to half of affected men. Depression and psychotic illnesses cause diminished sexual desire (but not necessarily loss of function) in a high proportion of both men and women, but careful questioning is needed to elicit them. Altered sleep pattern is a valuable indicator of depression. Heart disease, especially when combined with hyperlipidemia and arteriopathy, accounts for erectile dysfunction in many men. Other hormone deficiencies, especially thyroid and testosterone, reduce sexual desire and performance in both sexes. Operations and trauma, especially gynecological and urological, can cause sexual problems. Damage to the pelvis or spine is another obvious cause. Prolactinoma may, rarely, present with a loss of sexual desire and headaches in a younger man. Pain of arthritis, vaginal atrophy in the older woman or a phimosis may be off putting to one or other partner.

Medical and recreational drugs

Many drugs, especially hypotensives agents, alcohol, nicotine and many over the counter medications, that contain anticholinergics properties, can have a profound effect on sexual performance.

Table 1 *Commonly prescribed drugs associated with sexual dysfunction (list not fully comprehensive)*

Drug	Erectile dysfunction	Altered drive	Ejaculatory disorder	Orgasmic disorder	Priapism
Anticonvulsants					
Carbamazepine	X				
Phenytoin	X	X			
Primidone	X	X			
Antidepressants					
Tricyclics					
Amitriptyline	X	X	X		
Amoxapine	X	X	X		
Clomipramine	X	X	X	X	
Imipramine	X	X	X	X	
Maprotiline	X	X			
Nortriptyline	X	X			
Protriptyline	X	X	X		
Monoamine oxidase inhibitors					
Phenelzine	X	X	X	X	
Selective serotonin reuptake inhibitors					
Fluoxetine	X		X		
Fluvoxamine	X		X		
Paroxetine	X		X		
Sertraline	X		X		
Antipsychotics					
Chlorpromazine	X	X	X		X
Fluphenazine	X	X	X		
Haloperidol	X		X		
Thioridazine	X		X	X	X
Benzodiazepines	X	X	X	X	
Antihypertensives					
Atenolol	X				
Clonidine	X		X	X	
Guanethidine	X	X	X		
Hydralazine	X				X
Labetalol	X	X	X		X
Methyldopa	X	X	X	X	
Metoprolol	X	X			
Pindolol	X				
Prazosin	X				
Propranolol	X	X	X	X	
Reserpine	X	X	X		
Timolol	X	X			
Verapamil	X				
Diuretics					
Amiloride	X	X			
Chlorthalidone	X	X			
Indapamide	X	X			
Spironolactone	X	X			
Thiazides	X				
Antiemetics					
Metoclopramide	X	X			
Non-steroidal anti-inflammatory drugs					
Naproxen	X		X		
Anticholinergics					
Atropine	X				
Diphenhydramine	X	X			
Hydroxyzine	X	X			
Propantheline	X				
Scopolamine	X				
Antispasmodics					
Baclofen	X		X		
Hypnotics					
Barbiturates	X	X	X		

Inadequate hormone replacement therapy in menopausal women can cause vaginal atrophy and dryness leading to pain during sexual intercourse. This may not be volunteered by, or even be apparent to, her partner and is a good reason to try to listen to the couple together.

Cannabis can cause an initial euphoria, improving sexual confidence, but, like alcohol, it can greatly diminish performance. Other drugs, including the so called hard drugs, have a deleterious long term effect on sexual performance. Commonly prescribed drugs associated with sexual dysfunction are listed in Table 1.

Talking with the couple

Marital dysfunction or just plain sexual boredom after many years of being together can be a major cause of erectile dysfunction. In men with erectile dysfunction it is helpful to know the patient's, and especially his partner's, views of the causes. This often reveals their anxieties about other problems, as well. It is also useful to know the speed of onset: organic causes such as diabetes tend to develop slowly whereas psychogenic ones tend to appear more rapidly.

A psychogenic cause of erectile dysfunction is considered when the patient becomes erect during the night or upon early morning waking or if he can masturbate successfully, although many are reluctant to admit this in front of their partner. (Erectile dysfunction is covered in a later article in Toolbox)

Strains on the relationship

Strict upbringing and religious beliefs, especially if there is disparity between the partners (as in mixed marriages), can often have a devastating effect on a sexual relationship. Other issues to consider that add strain on sexual relations include unemployment (or the threat of it), retirement (through loss of self esteem) and menopause. Has the menopause or a hysterectomy changed the way a woman perceives herself? Does she feel less feminine or attractive to her partner? These aspects may need very tactful questioning to elicit, and require sensitivity on the part of the doctor.

Nonbeneficial or futile medical treatment: conflict resolution guidelines for the San Francisco Bay Area

By the Bay Area Network of Ethics Committees (BANEC) Nonbeneficial Treatment Working Group*

Correspondence to:
Steve Heilig
heilig@sirius.com

Sean Ellis/Tony Stone Images.

The need and potential for area-wide guidelines

Most people now die in a health care setting, so that decisions about when to terminate medical treatment are common. Many patients approach death without leaving instructions as to their desires. Surrogate decision-makers such as family members may disagree among themselves and with caregivers as to when "enough is enough." Stalemate situations are increasing, especially where the clinicians feel a patient cannot improve but families insist on invasive medical treatment and/or life support measures. The concept of "medical futility," is as old as Hippocrates. A growing literature has tried to develop clinically useful standards for arriving at a definition of non-beneficial treatment, ethical standards for decision-making, and dispute resolution procedures.

Methods for gaining consensus

The Bay Area Network of Ethics Committees (BANEC), an informal network of clinicians and others interested in the ethics of healthcare (members at meetings represent approximately thirty healthcare institutions throughout the San Francisco Bay area), began presenting meetings on nonbeneficial care in 1995.

A working group of 10 representatives of ethics committees from various Bay Area health care institutions drafted the following guidelines, which have had input from open review meetings attended by over 100 BANEC participants. The guidelines are now offered for consideration by any institution confronting this topic. When institutions develop such guidelines, they should be put on the public record and disseminated in the community. We would recommend public input wherever such policies are developed.

These guidelines intend to reflect the best standards of the medical profession in making difficult decisions about limits to treatment, especially when it is judged that specific treatments are not, or would not be, in the physicians' professional opinion, in the best interests of the patient. We recognize that legal risk management is likely to be a concern, but it is our conviction that medical concerns are the basic standard for decisionmaking. Use of the institutional ethics committee, with broad representation including community membership, is recommended primarily to increase communication among everyone involved in such cases.

Conflict resolution guidelines

1. Defining nonbeneficial treatment

Nonbeneficial treatment is any treatment that, in the best judgment of medical professionals, produces effects that cannot reasonably be expected to be experienced by the patient as beneficial, or to accomplish the patient's expressed and recognized medical goals; and/or will probably cause harm that outweighs any expected benefits. Potential examples of nonbeneficial treatment that have been raised for discussion include: (a) Provision of life sustaining treatment to a patient who is irreversibly unconscious; (b) Provision of any treatment other than comfort care when a patient has requested only comfort care; (c) Provision of indeterminate, long-term treatment to a patient who has no realistic chance of surviving outside an acute care hospital intensive care unit.

2. Determination of nonbeneficial treatment

The physician responsible for the care of the patient is responsible for making a determination that an intervention is medically nonbeneficial, and therefore inappropriate. When the physician and consultants, supported by the medical literature, conclude that further treatment (except comfort care) cannot, with reasonable probability, benefit the patient, such treatment may be judged to be nonbeneficial. When such a judgment

Family members may all be involved in end-of-life decisions. *Robert Bergin/Stock Illustration Source, 16 West 19th Street, New York, NY 10011; e-mail sis@sistock.com.*

Case histories

(Cases provided by Lawrence Schneiderman, MD and Steve Heilig, MPH, based upon composites of real cases. Details have been altered to protect confidentiality).

CASE 1

A 35-year-old homeless diabetic Caucasian man is found unconscious with severe hypoglycemia. Despite maximal life-saving treatments, he remains in a persistent vegetative state. No family or friends can be found. A decision must be made as to whether to keep him on life-sustaining treatment, consisting of tube-feeding and insulin with close monitoring.

This case illustrates both the problematic medical/legal environment in this country and the usefulness of procedural guidelines. The patient's physician obtained a neurological consultation. The neurologist concluded, after 3 months had passed, that the patient was in a permanent vegetative state and had no reasonable chance of regaining consciousness. The patient's physician proposed that, since the hospital had a futility policy that defined life-sustaining treatment of a permanently unconscious patient as futile, that tube feeding and insulin be discontinued. The hospital risk manager insisted that treatment be continued until a guardian could be appointed by local authorities, who could then make a court-supported decision on behalf of the patient. The physician objected that such a process could take months, and argued that the existing care team could represent the patients' interests just as well as an appointed guardian. The physician asked the ethics committee to review the case. The whole committee, made up of hospital and community representatives, supported the physician's position. It proposed that the patient be transferred to a hospital whose policy did not define life-sustaining treatment of a permanently unconscious patient as futile, or to a skilled nursing facility. If no such transfer could be arranged, the physician was entitled to withdraw life-sustaining treatment in accordance with hospital policy.

has been made, a recommendation to withhold or withdraw the intervention should result, and the following should occur, at a minimum:

A. Patients with medical decision making capacity should be informed of the judgment, the medical rationale supporting it, and the alternatives and their likely outcomes. The physician should explain that withholding or withdrawing the intervention still means appropriate medical and humane care will be provided.
B. For patients without decisionmaking capacity, the discussion and understanding as described above should be sought from a surrogate decisionmaker. If surrogates cannot be located, the physician, after appropriate consultation, should be able to make decisions regarding discontinuation of treatment. When multiple surrogates are available but in conflict, a single surrogate should be chosen. In all cases, the surrogate should provide evidence that the surrogate's position is in accord with what the patient would desire, or if such desires are unknown, are consistent with the patient's values.

If consent is obtained, the treatment may be withdrawn or withheld in compliance with the applicable procedures of the institution.

3. Procedures in cases of lack of consent regarding nonbeneficial treatment

Where there is disagreement on the course of the patient's treatment between the physician and the patient and/or the patient's surrogates, a consultation with another appropriate physician shall be offered. The patient or surrogate shall be consulted regarding the choice of a physician for this second opinion.

A. If, after reviewing the patient's case and speaking with the patient and/or surrogates, the second physician disagrees with the primary physician, the patient and/or surrogate shall be informed of this difference in opinion and, wherever appropriate and possible, offered transfer to another physician's care and/or to another institution.
B. If, after reviewing the patient's case and speaking with the patient and/or surrogates, the second physician agrees with the primary physician that nonbeneficial treatment should be withheld or withdrawn, the patient and/or surrogates shall be informed of this second opinion. If the patient and/or surrogate now agrees with the two physicians, the intervention in question will be withdrawn or withheld in accordance with the institution's accepted policies and procedures.

Where disagreement persists between the primary physician and the patient and/or surrogate, the following procedures shall be followed.

1. The patient will be offered consultation with additional institutional or other resources as appropriate, (such as the ethics consultation service or consultant).
2. If disagreement persists, the physician shall present the case for review by an institutional ethics committee or other body for a recommendation regarding the patient's treatment. The review committee membership should include not only relevant institutional expertise, but external community representatives without financial interest in the institution or individual case.
3. The patient and/or surrogate shall be informed (in sufficent time) of the meeting and and invited to attend to present the patient's perspective. Anyone, including members of the caregiving team, who has a direct stake in the patient's care should be considered potential participants.
4. The review committee shall offer a recommendation on the case following the meeting. The recommendation shall reflect a consensus opinion of the committee, with no major disagreement, if nonbeneficial treatment is to be withheld or withdrawn (A specific minimum majority vote may be established as a criteria in such cases, such as requiring that 75% of voting members support the determination of nonbeneficial treatment). The committee's opinion shall be considered as an advisory and nonbinding recommendation for use by the primary physician and others involved in decision making in the case. The recommendation shall be accurately recorded in the committee minutes.
5. If the review committee agrees with the physician's determination of nonbeneficial treatment, the patient and/or surrogate shall be promptly informed of this decision. Surrogates shall be informed of all options available other than continuing treatment, including legal procedures (such as court orders compelling continued treatment) and transfer. If transfer to another institution is desired by the patient and/or surrogate, such transfer will be facilitated as possible. If transfer is not possible, a plan for withholding or withdrawal of nonbeneficial treatment may ethically be made, emphasizing the provision of comfort care and preservation of patient dignity.
6. If the review committee does not concur with the physician's recommendation, that physician should give serious consideration to the recommendation that treatment shall not be withheld or withdrawn or otherwise limited without patient or surrogate consent. Arrangements for transfer to another physician's care will be made if requested by either the physician or patient and/or surrogate. The current physician shall make a good faith effort to find

CASE 2

A 70-year-old African American woman is severely obtunded with multiple diseases, including heart disease, stroke, diabetes, peripheral vascular insufficiency and chronic obstructive lung disease. She cannot participate in medical decisions and is deteriorating despite maximal treatments. Her daughters, nieces, and sister, all claiming they know the patient best, disagree vehemently about how aggressively she would want to be treated. The patient has designated no surrogate decision-maker and has expressed contradictory wishes in the past. Decisions must be made about whether to perform a tracheostomy to maintain her life-sustaining ventilation, how aggressively to treat life-threatening infections, including whether to amputate her compromised extremities, and whether or not to attempt CPR in the event of a cardiac arrest.

In this case, the patient's physician felt that she should order no code-comfort care only. Some family members disagreed, so the physician requested a second opinion, which confirmed her prognosis and treatment plan. Disagreement among the family persisted. The family was invited to bring in their own consultant, but they could not agree on any. The physician requested an ethics consultation. During this meeting, which included family members and the patient's care team, the patient's condition and prognosis were reviewed in detail, and efforts were made to have the family agree on a patient surrogate. This meeting failed to achieve consensus among the family.

Further dispute resolution was attempted in a meeting involving the patient's physician and nurses, family members, and the full ethics committee. This also failed and while the committee could not agree who best represented the patient's wishes it agreed that changing the patient's treatment emphasis from aggressive life-support to comfort care was motivated by the patient's best interests and therefore was ethically defensible. The family was presented with these results of the ethics committee's deliberation, and offered counseling during a 72-hour grace period before no-code status was ordered, seeking transfer to another institution, or a court order to compel treatment. During this time, efforts were made to provide counseling, and the family was assured that the full code status would remain in place.

When transfer was not possible, the family debated what to do even as the no code order was written. The care team agreed to follow the patient for at least one more week to accommodate the family's grieving before removing the ventilator. During that time the patient developed overwhelming sepsis, which was not aggressively treated, and she died. Although one family member threatened legal action, he did not follow through on this threat.

another appropriate physician to undertake the patient's care. Until that is accomplished, the current physician is ethically and legally responsible for the care of the patient.

Sources

Alexian Brothers Hospital. Non-Beneficial Treatment. Policy #MS006092, 1997 (San Jose, CA).

Alta Bates Medical Center. When a Physician and Patient Disagree About the Benefits of Treatment. Proposed addendum to DNR Policy, 1999. (Berkeley, CA).

American Medical Association, Council on Ethical and Judicial Affairs, 1998-1999. Code of Medical Ethics. Current Opinions with Annotations (See 2.035: Futile Care).

American Medical Association, Council on Ethical and Judicial Affairs Guidelines for Ethics Committees in Healthcare Institutions. *JAMA* 1985; 253:2698-2699.

American Thoracic Society Bioethics Task Force. Withholding and withdrawing life-sustaining therapy. *Ann Int Med* 1991; 115:478-485

Bay Area Network of Ethics Committees. Termination of Life Support: Guidelines for the Development of Institutional Policy. 1989. (San Francisco, CA).

California Medical Association. Futile Medical Treatment. A White Paper Prepared by the Committee on Bioethical Issues, 1996.

Halevy A, Brody BA. A Multi-institution collaborative policy on medical futility. *JAMA* 1996; 276(6):571-574.

Jecker NS, Schneiderman LJ. Medical Futility: The duty not to treat. *Cambridge Healthcare Ethics* 1993; 2:151-159.

Luce JM. Physicians do not have a responsibility to provide futile or unreasonable care if a patient or family insists. *Crit Care Med* 1995; 23:760-766.

Luce JM. Making decisions about the foregoing of life-sustaining therapy. *Am J Respiratory Critic Care, Med* 1997; 156:1715-1718.

Riven, AU. Futile Care Policy: Lessons learned from three years' experience in a community hospital. *West J Med* 1997; 166:389-393.

Sacramento Healthcare Decisions. Community Recommendations for Appropriate, Humane Medical Care for Dying or Irreversibly Ill Patients. 1997.

San Francisco General Hospital. Withholding and Withdrawal of Medical Treatments. Policy # 12.01, 1992 (San Francisco, CA).

Santa Clara County Medical Association. Prototype for Nonbeneficial Treatment Guidelines. 1996.

Schneiderman LJ, Manning S. The Baby K case. *Camb Q Healthcare Ethics* 1997; 6:91-18.

Schneiderman LJ, Jecker NS, Jonsen AR. Medical Futility: Response to critiques. *Ann Int Med* 1996; 125:669-674.

Schneiderman LJ, Jecker NS. *Wrong Medicine: Doctors, Patients, and Futile Treatment.* Johns Hopkins University Press, 1995.

Smith GP. Restructuring the principle of medical futility. *J Palliative Care* 1995; 11:9-16.

Society of Critical Care Medicine. Consensus Statement regarding futile and other possibly inadvisable treatments. *Critical Care Med* 25:887-891.

Note: This document represents suggested guidelines for potential policy to be used as appropriate by individuals or organizations. The Bay Area Network of Ethics committees provide a forum for open, independent discussion of ethical issues in healthcare. Opinions and guidelines proferred via BANEC are not necessarily representative of or endorsed by any organization participating in BANEC activities, and are nonbinding. Comments on BANEC policies are welcomed.

Funding provided by the Walter and Elise Haas Fund, the Wallace Alexander Gerbode Foundation, and the San Francisco Medical Society Community Service Foundation.

*Steve Heilig, William Andereck, Robert Brody, Sister Patrice Burns, John Luce, San Francisco, CA; William Kennedy, Salinas, CA; John Longwell San Jose, CA; Alice Mead, Mill Valley, CA; Guy Micco, Berkeley, CA. (Among those who contributed, special thanks are due to Lawrence Schneiderman, Wesley Jan, Gene Eldredge, Bruce Bartlow, Theresa Drought, David Allen, Sallie Allen, Newton Harband, and three anonymous reviewers Listing of these reviewers does not imply endorsement of the final guidelines).

COMMENTARY

Why futility policies are not the answer

Susan B Rubin, The Ethics Practice, Berkeley, CA. Dr Rubin is author of *When Doctors say No: The Battleground of Medical Futility* (Indiana University Press, 1998).

Imagine a world in which physicians, supported by an array of institutional resources, could finally say no to the unreasonable demands of their patients—in which a clear community standard would support the use of professional judgement to limit inappropriate care. It is a world envisioned by many futility policies. But before falling prey to the seductive power of these policies and the movement behind them, we must examine their flawed premises and consider the implications of their adoption.

First, most policies are professionally driven though there is no evidence that the lay population would sanction the medical profession's approach to these questions. To be defensible, such policies must take into account not just the profession's but also the broader community's perspective as well.

Why? Because medicine is not only a moral enterprise—it is also a social practice.

Second, any approach to futility must consider what protection will be given to minority perspectives. A striking feature of many futility conflicts is that they involve religiously motivated requests for treatment deemed futile by the treating physicians. What should the standing of these faith claims be? This is a question for society to resolve, not just the medical profession.

Third, any proposal to limit treatment on the basis of futility must establish meaningful recourse for patients who disagree with their physicians. Too often the strategy is to stipulate the outcome in advance or to focus on securing patient acquiescence. Seldom do policies create genuinely open-ended processes for reflection, in which answers are forged collectively.

The guidelines by the Bay Area Network of Ethics Committees read like a decision tree aimed at bringing the patient on board. Progressive interventions are triggered by the patient's—not the physician's disagreement. The interventions are all good but seem intended to secure the patient's agreement with the physician. The ethics committee functions almost as a final green or yellow light for physicians. If the committee agrees with the physician the presumption is the physician will prevail unless the patient goes to court or facilitates transfer. It is not acknowledged that going to court is too costly for many patients or that transfer in this age of managed care is not realistic. At no point is there mention of physicians reconsidering their position or of the steps physicians might need to take, such as going to court, to prevail in the end. If the committee disagrees with the physician, it is suggested the committee's recommendation be seriously reconsidered while transfer is explored. The existing imbalance of power between physicians and patients is only underscored by such an approach.

What we need instead of such policies is an approach that encourages meaningful open-ended conversation between physicians and patients and broad social discourse about the genuine issues at stake. Unfortunately this is precisely the sort of thing policies can't do.

COMMENTARY

Respect for patients should dominate health care decisions

Ann Alpers, Department of Medicine, University of California, San Francisco, CA; anna@medicine.ucsf.edu

Patients and their families sometimes disagree with physician recommendations concerning end-of-life care. They may reject the physicians' pessimism, they may accept a different quality of life, or they may value sustaining a loved one's life in ways that the physicians do not understand. Intractable disagreements, while rare, occur.[1] The search for a widely accepted substantive definition of futility has, in its own way, been futile.[2]

The conflict resolution guidelines crafted by BANEC are a recent, important addition to the growing number of community policies to promote ethical and rational resolution of disputes about medical futility.Their most useful contributions are likely to be their emphasis on straightforward communication with patients or their surrogates and their procedures for resolving disagreements. The guidelines reject unilateral action by a physician by requiring consultation by another physician and further review by an institutional group, like the ethics committee, that has community members as well as hospital staff. The guidelines stress physicians' obligation to provide excellent palliative care and call for the involvement of social workers, chaplains, and other caregivers who may be better at resolving conflicts than the treating physicians.

One persistent question about futility policies is: will they work?[3] What would a well-designed study measure to attempt an answer? From the perspective of patient autonomy, one might wonder whether guidelines like those of BANEC's working group promote patient or family satisfaction. From the perspective of distributive justice, one might wonder whether such guidelines reduced the length of stay of patients who died in the hospital. Other measures of quality of care could include the number of days patients spent on a ventilator or in intensive care before dying.[4]

An important measure of the BANEC guidelines' success is effective conflict resolution. One marker of the bitterness of conflict may be whether legal actions flow from unresolved disagreements. Malpractice suits can arise out of a futility dispute. In a malpractice suit concerning futility, evidence about the standard of care would be presented in court. This evidence would help a jury determine whether a physician had a duty to provide the disputed treatment or to take certain procedural steps before withholding or stopping it. Community policies might serve as a new source of such evidence[5] because courts look to statements by professional groups and institutions that define standards of practice as one of the main sources of the legal duties to which members of the medical profession must conform.[6,7] Nevertheless, the success of community guidelines in protecting physicians from malpractice judgments remains untested.

In *Gilgunn v. Massachusetts General Hospital,* the jury decided that physicians were not negligent when they decided to withdraw mechanical ventilation and issue a do not attempt resuscitation order despite the objections of the patient's daughter.[8] *Gilgunn* contrasts with *In the Matter of Baby K,* in which physicians and a hospital attempted to insulate themselves from liability by requesting judicial permission to withhold mechanical ventilation from an anencephalic infant.[9] Physicians are likely to get better legal results when they refuse to provide nonbeneficial treatment and then defend their decisions as consistent with professional standards than when they seek advance permission to withhold care. As George Annas has warned, "Physicians cannot expect…trial-court judges…to take practice standards more seriously than they do themselves."[10] If community guidelines provide reassurance that physicians and risk managers can successfully defend malpractice suits, such guidelines may support the ethical value of professional integrity.

The BANEC guidelines recommend one specific technique to reduce conflict. They note that when a patient lacks the capacity to make medical decisions, several surrogates may be available but in conflict. Conflict between potential surrogates occurs often enough to be its own syndrome.[11] The guidelines suggest that a single spokesperson should represent the surrogates, but do not define a means for selecting among them. Any legal next of kin would have standing to sue for malpractice—although the suit might not progress very far—or to seek other legal means to thwart the withholding of life-sustaining treatment. Part of an inclusive mediation model for resolving conflicts should include fair procedures for all concerned. Some families, communities, and cultures may have traditions for selecting spokespersons but caregivers and review committees should be prepared to speak directly with any surrogates who have legitimate interests in the patient's care.

The BANEC guidelines insist that professional integrity and respect for patients, both as individuals and as members of a community, not concerns about legal liability or individual egos, should dominate decisions about care. This insistence can only improve our debate. Taking good care of the dying is hard but talking about it may be getting easier.

References

1. Prendergast T, Luce J. Increasing incidence of withholding and withdrawal of life support from the critically ill. *Am J Respir Crit Care Med* 1997; 155:15-20.
2. Curtis J, Park D, Krone M, Pearlman R. Use of the medical futility rationale in do-not-attempt-resuscitation orders. *JAMA* 1995; 273:124-128.
3. Spielman B. Community futility policies: the illusion of consensus? In: Zucker M, Zucker H, eds. *Medical Futility and the Evaluation of Life-Sustaining Treatment.* Cambridge, UK: Cambridge University Press, 1997; 168-178.
4. The SUPPORT Principal Investigators. A controlled trial to improve care for seriously ill hospitalized patients. *JAMA* 1995; 274:1591-8.
5. Schneiderman L, Manning S. The Baby K case: a search for the elusive standard of medical care. *Cambridge Q Healthcare Ethics* 1997; 6:9-18.
6. Kapp M. ACookbook@ medicine: a legal perspective. Arch Int Med 1990; 150:496-500.
7. Capron A. Abandoning a waning life. *Hastings Center Report* 1995; 24:24-26.
8. *Gilgunn v. Massachusetts General Hospital,* No. 92-4820 (Mass. Super. Ct. Civ. Action Suffolk Co. April 22, 1995).
9. *In the Matter of Baby K,* 16 F.3d 590 (4th Cir. 1994).
10. Annas G. Asking the courts to set the standard of emergency care—the case of Baby K. *N Engl J Med* 1994; 330:1542-1545.
11. Molloy D, Clarnette R, Braun E, Eisemann M, Sneiderman B. Decision making in the incompetent elderly: "the daughter from California syndrome." *JAGS* 1991; 39:396-99.

capsule

Air travel can be safe for patients with unstable angina American military personnel living in Japan, Korea, or Taiwan often choose to be airlifted out when they get sick. But if they have unstable angina, is it safe for them to fly? Yes, so long as its not on a commercial airline (*Aviation, Space and Environmental Medicine* 1999; 70;103-5). Reassuringly, 59 patients with unstable angina were carried home for cardiology assessment from the Pacific area between 1992 and 1996 without serious mishap. Two complained of chest pain and one of a headache.

Therapeutic effectiveness and social context: the case of lobotomy in a California state hospital, 1947-1954

Joel Braslow
Department of Psychiatry and Biobehavioral Sciences and History, University of California, Los Angeles, CA

Correspondence to:
Dr Braslow
jbraslow@ucla.edu

Introduction

That social and cultural values and beliefs play an integral part in physicians' medical practices has long been acknowledged.[1,2] Nonetheless, we often lose sight of this fact in contemporary medicine, especially as our knowledge and interventions appear to be increasingly based in science and less upon the vagaries of the sociocultural context.[3] But in every era, physicians generally believe that they have based their therapeutic decisions upon the firm bedrock of their contemporaneous science.[4,5] Given that our predecessors most likely had as much faith in their treatments as we do in ours, history can help us to expose the ways in which physicians incorporate the social and cultural world into their medical practices. By studying a therapy that is no longer used, we can step out of our "time and place" bias, where our surrounding culture and clinical presuppositions are often uncritically accepted, and explore a treatment without inserting our own preconceptions. To this end, this essay examines how physicians' use of a Nobel Prize winning intervention reflected both institutional needs and cultural values concerning women, illustrating howe the social world can become an indivisible part of what physicians' deem as disease and therapeutic effectiveness.

Specifically, we will explore doctors' use of lobotomy in a California state hospital between 1947 and 1954. Not only were state hospital physicians subject to obvious institutional constraints,[6-8] but study of a now discredited therapy such as lobotomy allows us to examine the ways in which physicians constructed effectiveness. Since few currently would argue that lobotomy worked, we do not need to concern ourselves with the thorny problem of efficacy.[9] I performed a quantitative and qualitative analysis of the medical records of patients who underwent this procedure. In addition to the usual contents of a medical record, these records also contain verbatim transcripts of patient interviews, which were performed on admission and on consideration of a major therapeutic intervention.

History of the surgery

Let us first briefly review the history of this surgery, which, for our purposes, begins in the early 1930s. Based on several decades of experimental and clinical evidence, the Portuguese neurologist Egas Moniz speculated that fixed neuronal connections in the frontal lobes led to psychiatric disease, and that disruption of these connections could lead to cure.[10-12] In 1935, Moniz tested this theory on a psychiatric patient by severing the frontal white matter projections with multiple injections of alcohol into the frontal lobes, thus giving birth to the first modern frontal lobotomy.[13] Despite some opposition, the treatment eventually gained widespread legitimacy and became part of mainstream medical practice.[14] Underscoring its scientific acceptance, the Nobel Prize Committee awarded Moniz the 1949 prize in physiology and medicine.[15] As a result of these scientific credentials, physicians throughout the United States began using the remedy. By 1950, for example, the surgery was performed in 286 hospitals in the United States and, by 1951, an estimated 18,000 patients had undergone the operation.[16]

Medical record review

The site of my medical record review was Stockton State Hospital, located about 30 miles southeast of Sacramento. Opened in 1851, Stockton is the oldest psychiatric institution west of the Missouri River.[17-19] Just before the introduction of lobotomy into Stockton, over 4,000

Egaz Moniz—inventor of the lobotomy. *With permission from US National Library of Medicine.*

Summary Points

- Physicians believe they base their therapeutic decisions on science but in fact incorporate social and culture issues into their medical practices
- The practice of lobotomy in the late 1940s and early 1950s illustrates some of the ways in which physicians employ sociocultural factors in their medical treatment of patients
- Records of lobotomized individuals from a California state psychiatric institution show that between 1947 and 1954 the social problems of hospital management (especially the need for order) determined what physicians saw as disease and how they measured therapeutic success or failure
- Lobotomizing over five times as many women as men, physicians at this institution also incorporated prevalent cultural views concerning women in their practice of lobotomy, both in how they determined surgically treatable psychiatric disease and how they measured a woman's response to the surgery

patients lived behind its walls, treated by 11 physicians.[20] Not surprisingly, given this overwhelming, although not unique, patient to doctor ratio, physicians placed an extremely high value on maintaining order within the asylum. Uncontrollable patients not only posed vexing clinical problems but severely taxed the staff's meager resources, often compromising the care of other, more compliant patients. Nonetheless, physicians did possess a variety of technologies with which to maintain order: these included electroconvulsive therapy, hydrotherapy, mechanical restraints, and chemical restraints (such as barbiturates and hyoscine).[21] Despite this array of interventions, some patients proved unresponsive. It was against this background that physicians' use of lobotomy reflected their institutionally dictated need for order. This context also provided a fertile ground for physicians to see women as more likely surgical candidates than men.

Between March 1947 and June 1954, physicians performed 245 lobotomies on 232 patients. They abruptly terminated their lobotomy program with the introduction of the antipsychotic drugs reserpine and chlorpromazine in 1954. Since a number of case files were either lost or misplaced, 147 patient records were available for review. In what follows, I will show how doctors' use of lobotomy reflected their vision of proper gender roles for women. First, however, I will present typical verbatim comments culled from a careful reading of these available records to illustrate how physicians transformed an institutional imperative into a matter of individual therapeutics.

Social control and medical treatment

For Stockton physicians, lobotomy was simultaneously a method of patient management and ward management. Emphasizing the social aspect of psychiatric disorder, doctors at Stockton defined surgically treatable disease as uncontrollable behavior. And they most commonly cited those behaviors that disrupted the ward routine and occupied the attendants and nurses as the kind in most dire need of surgery. Thus, not surprisingly, physicians saw little difference between what benefited the individual patient and what benefited the ward. The following case illustrates how doctors saw lobotomy as a solution for both social and individual problems.[22]

The patient, a 40-year-old woman, had undergone two previous radical lobotomies but continued to display "extremely perverse behavior." In recommending a third lobotomy, her ward physician wrote:

> A transorbital variety of prefrontal leukotomy has not yet been tried and it is recommended... [T]here is a hope that personnel may be released for more useful work elsewhere if not required to continually supervise and restrain this patient.[23]

Furthermore, physicians determined a successful or unsuccessful outcome by how well a lobotomized patient adapted to the ward routine as this next example illustrates:

> Six months [after lobotomy] she was still... restless, assaultive toward others and herself... kicking and fighting anyone who came near... antagonistic, she screams and throws anything she can get ahold of... The question is, would a second radical prefrontal be of any help?[24]

The staff's continued inability to control this woman's violence constituted her physician's primary measure of the treatment's effectiveness. Significantly, the first lobotomy's failure did not shake the doctor's belief in the surgery as a means of behavioral control. Shortly after this note was written, the patient underwent a second lobotomy.

Doctors' focus on institutional needs instead of than the individual patient often created what appear in hindsight as some curious measures of therapeutic success. For example, a frequent side effect of frontal lobotomy was that patients became apathetic and indifferent, lacking any of their previous emotional spontaneity.[25-28] However, since conformity to ward routine measured therapeutic success, Stockton physicians transformed these neurologic sequelae into measures of effectiveness, as this discussion between several physicians suggests:

> **Dr. A:** [Before lobotomy] she was regressed an awful lot—she was in restraint most of the time, would spit at people and break things up.
> **Dr. B:** [Lobotomy] leaves them all pretty flat and indifferent about things. It seems to be characteristic—

Dr. A: There is not much animation any more.
Dr. C: Maybe that is what cures them.[29]

For these doctors, "cure" had as much to do with conserving the institution's precious staff resources as with addressing this woman's individual needs.

Gender and Therapeutics

Focusing on gender, let us now take a quantitative look at Stockton's Lobotomy program. Of the 241 patients where sex could be identified from the surgical summaries, 205 (85%) were women and 36 (15%) were men. Demographics cannot account for these differences. Men not only outnumber women within the hospital, but they also predominated in the diagnostic categories that physicians most commonly lobotomized, schizophrenia being by far the most frequent diagnosis given to a surgical candidate. It is also worth noting that one third of the physicians who participated in the lobotomy program were women. Interestingly, I found that these gender differences were present only in these doctors' use of lobotomy. In the case of electroconvulsive therapy, doctors treated an equal number of women and men as is evident from a sample of 400 randomly selected records with admission dates roughly equaling those of the lobotomy sample. In this sample, the relative frequencies with which women underwent electroconvulsive therapy equaled that of men. Similarly, I found no evidence that doctors used other remedies, such as hydrotherapy or malaria fever therapy, on women more often than men.

How can we account for these gender differences? While it is possible that these physicians were simply misogynistically acting out their greater desire to control and subjugate women rather than men, a causal explanation is difficult to prove. However, irrespective of the source of these marked differences, physicians incorporated their views concerning the social roles of women into what they considered medical indications for lobotomy and their assessments of the effectiveness of the surgery Through this process, physicians transformed social values into problems of medical management, a process vividly illustrated by what doctors at Stockton actually said to their patients and their patients' loved ones.

For example, doctors often saw a woman's inability to conform to expected social roles as evidence of psychiatric disease. Let us listen in on a conversation between a physician and his patient. In this case, the doctor successfully ferrets out telltale signs of operable psychiatric disorder.

Doctor: Why haven't you been looking after the children better than you have?
Patient: I was working for the telephone company.
Doctor: Was it necessary for you to work? Wouldn't it have been better for you to stay home and look after the children?
Patient: It might have been better.
Doctor: Why didn't you?
Patient: I intend to do better.
Doctor: It is strange behavior. First you don't stay with the children but go to work; now you are not with them [but] you want to be with them.
Patient: (No answer.)[30]

This "strange behavior"—that is the patient's ambivalence about taking care of her children—played an important part in the doctor's and his colleagues' decision to classify her as a psychiatric patient and their decision to lobotomize her.

These accepted social values about a woman's ideal role also provided doctors with a yardstick for measuring the success of the surgery. Although the neurological deficits caused by the procedure often made patients oblivious to their postsurgical psychiatric state, husbands frequently attested to their wives' recoveries. In the following dialogue we see that despite the patient's loss of spontaneity and individual desires, both the doctors and the patient's husband believed that these deficits posed little problem for her recovery.

(Patient dismissed)
Doctor: We want to get some idea from you how she has been [since the lobotomy].
Husband: I think she has been behaving wonderful.
Doctor: She doesn't seem to worry?
Husband: That is one thing. Before commitment she was awfully worried about everything. It was a continuous worry all the time but now she takes things as they come... She kind of watches over the house and cleans it and the only one thing she is not too particular about her appearance. She don't care what anybody says.
Doctor: That is one of the disadvantages of this operation she had.
Husband: I think it is for the best really because she doesn't worry at all about anything.[31]

Noting that "the husband is more satisfied," the staff discharged her as recovered. For this patient's doctors and her husband, her restoration as an ideal wife—that is, her ability to cook, clean, and do housework—was an integral part of her recovery. While her redemption as an "ideal woman" came at substantial personal cost, her husband and doctors saw this as a small price to pay when measured against social and institutional values.

Conclusion

Institutional and social factors intimately affect medical practice. For physicians at Stockton State Hospital, these factors determined what kinds of behaviors they saw as disease and how they measured therapeutic success. Based on the best biological science of the mid-twentieth century, this Nobel Prize winning therapy was as much a social technology as a medical one. But we should not be too harsh in our judgement of these doctors. Just as we are today, they and their science were enmeshed in a specific time and context in which social and medical values were part of the same world.

This project was supported in part by the VISN 22 Mental Illness Research Education and Clinical Center of the Department of Veterans Affairs and the Burroughs Wellcom Fund 40th Anniversary Awards for the History of Medicine.

Sources and References

1. Rosenberg CE. *The Cholera Years, the United States in 1832, 1849, and 1866.* Chicago: University of Chicago Press; 1962.
2. Rosenberg CE, Golden J (Eds). *Framing Disease: Studies in Cultural History.* New Brunswick (NJ): Rutgers University Press; 1992.
3. Aronowitz RA. *Making Sense of Illness: Science, Society, and Disease.* Cambridge (UK): Cambridge University Press; 1998.
4. Vogel MJ, Rosenberg CE. *The Therapeutic Revolution: Essays in the Social History of American Medicine.* Philadelphia: University of Pennsylvania Press; 1979.
5. Warner JH. *The Therapeutic Perspective: Medical Practice, Knowledge, and Identity in America, 1820-1885.* Cambridge (MA): Harvard University Press; 1986.
6. Grob GN. *Mental Institutions in America: Social Policy to 1875.* New York: Free Press; 1973.
7. Grob GN. *Mental Illness and American Society, 1875-1940.* Princeton (NJ): Princeton University Press; 1983.
8. Grob GN. *From Asylum to Community: Mental Health Policy in Modern America.* Princeton (NJ): Princeton University Press; 1991.
9. O'Callaghan MAJ, Caroll D. *Psychosurgery, a Scientific Analysis.* Ridgewood (NJ): G.A. Bogden; 1982.
10. Moniz E. How I succeeded in performing the prefrontal leukotomy. In Sackler AM, et al (Eds): *The Great Physiodynamic Therapies in Psychiatry; an Historical Reappraisal.* New York: Hoeber-Harper; 1956, pp 131C137.
11. Damasio AR. Egas Moniz, pioneer of angiography and leucotomy. *Mt Sinai J Med* 1975; 42: 502-513.
12. Black DW. Psychosurgery. *South Med J* 1982; 75:453-458.
13. Moniz E. Prefrontal leucotomy in the treatment of mental disorders. *Am J Psychiatry* 1936; 93:1379-1385
14. Pressman JD. *Last Resort: Psychosurgery and the Limits of Medicine.* Cambridge (UK): Cambridge University Press; 1998.
15. Valenstein ES. *Great and Desperate Cures: the Rise and Decline of Psychosurgery and Other Radical Treatments for Mental Illness.* New York: Basic Books; 1986.
16. Kramer M. The 1951 survey of the use of psychosurgery. In Proceedings of the Third Research Conference on Psychosurgery. PHS Publication 221. Washington, D. C.: United States Government Printing Office; 1954, pp 159-168.
17. Smyth MH. Psychiatric history and development in California. *Am J Psychiatry* 1938; 94:1222-1236.
18. Klotter A. California mental hospitals: an historical sketch. *Bull Med Libr Assoc* 1957; 45:159-163.
19. Brody S. Hospitalization of the mentally ill during California's early years: 1849-1853. *Psychiatr Q* 1964 (Supplement); 38:262-272.
20. California. Statistical report for the Department of Mental Hygiene, year ending June 30, 1947. Sacramento (CA): California State Printing Office.
21. Braslow JT. *Mental Ills and Bodily Cures: Psychiatric Treatment in the First Half of the Twentieth Century.* Berkeley: University of California Press; 1997.
22. In order to protect patient privacy, all numbers and identifying characteristics have been changed. I have retained the original spelling and punctuation in all of my quotations from the medical record. Records from Stockton State Hospital were at the Stockton Developmental Center until its closing in February of 1996. With appropriate permission from the California Department of Mental Health, one can obtain the actual patient record numbers from the author.
23. Stockton State Hospital case 47836, continuous notes, 23.
24. Stockton State Hospital case 53765, continuous notes, 17.
25. Ewald FR, Freeman WJ, Watts JW. Psychosurgery; the nursing problem. *Am J Nurs* 1947; 47:210-213.
26. Freeman WJ, Watts JW. Prefrontal lobotomy in the treatment of mental disorders. *South Med J* 1937; 30:23-31.
27. Cohen LH, Novick RG, Ettleson A. Frontal lobotomy in the treatment of chronic psychotic overactivity. *Psychosom Med* 1942; 4:96-104.
28. Aldrich, CK. Problems of social adjustment following lobotomy. *Am J Psychiatry* 1950; 107:459-462.
29. Stockton State Hospital case 51465, clinical conference, 3
30. Stockton State Hospital case 66222, clinical conference, 2.
31. Stockton State Hospital case 51078, clinical conference.

CDrom REVIEW

Current Medical Diagnosis and Treatment 1998

Stephen J McPhee, Lawrence M Tierney Jr, Maxine A Papadakis, Ralph Gonzales

Appleton and Lange, ISBN 0 8385 1480 4

Rating: ★ ★ ★

Price: $99.00

Can a reference source really meet the needs of "a student, resident or clinician," as the user's guide for this CD claims? To do so, the information it provides would need to be readily accessible, up to date, and capable of answering the questions that members of each of these groups might pose.

It is certainly quick. The questions I asked it in a week of seeing patients, preparing for teaching sessions, and reviewing grant applications convinced me of that. Whether I wanted to know about drugs, diseases, or diagnostic tests that were unfamiliar to me, the search engine usually found what I was looking for within 2 seconds (you don't even need to understand its Boolean search operators).

When I checked how current it was I was even more impressed. Every reference until the end of 1997 that I knew about was there with abstracts and hypertext links. I was unable to discover any omitted references without extending my searches beyond Medline.

Of course, the kinds of questions its three target groups ask vary considerably. Students and residents will like the accessible, authoritative text, and they will love the audio and video multimedia features. Cardiovascular and respiratory systems are well represented in these features, with less detail on other systems.

The system's functionality goes beyond the limitations of other CD Roms by providing facilities for updating and personalizing the material it contains. The database may be continuously updated via links to 200 internet addresses. Individuals can tag and bookmark the material that is relevant to them.

Many students, residents, and even clinicians don't yet have uninterrupted access to a computer with a CD Rom. Perhaps the availability of reference material like this will encourage more information technology managers to invest in giving their students and clinicians the rapid, relevant access they need to practice evidence based medicine.

—Frank Sullivan, *Professor of research and development in general practice and primary care,* Tayside Centre for General Practice, Dundee University

wjm

ern journal of medicine

- Re-launched
- Re-vitalized
- Re-worked
- The education resource for clinicians in Western States

Subscription rates

Individual
$70 US/Canada;
$85 Outside US/Canada

Institutional
$120 US/Canada;
$130 Outside US/Canada

Student, group and association rates available

Contact our Subscription Hotline on
1-800-236-6265

Fax
1-800-232-9265

Email
bjpaige@cybertours.com

MONEY BACK GUARANTEE • CANCEL AT ANY TIME AND YOU WILL RECEIVE A REFUND ON ALL UNMAILED ISSUES

Stay Informed...Subscribe Today

WJM Western Journal of Medicine

Publication: Monthly ISSN 0093 0415

1999 SUBSCRIPTION RATES

- ☐ Individual rate: $70 US/Canada; $85 Outside US/Canada
- ☐ Institutional rate: $120 US/Canada; $130 Outside US/Canada
- ☐ Start Issue..... (month/year)
- ☐ Send me Guidelines for Authors

My primary speciality is.....

Years in practice .....

- ☐ I enclose a check for $..... (Payable to Western Journal of Medicine)

US Dollar checks to be drawn on a US bank account.

...../...../...../.....

AMEX/Visa/Mastercard/ (delete as appropriate)

Expiration date .....

Signature ..... Date .....

(Your signature is essential when paying by credit card)

Name .....

Address .....

(Please print your billing address)

.....

.....

City .....

State, Zipcode .....

Return to:

WJM, PO Box 590A, Kennebunkport, ME 04046,
Phone: 1-800-236-6265 Fax: 1-800-232-9265
Email: bjpaige@cybertours.com

WJM Western Journal of Medicine

Publication: Monthly ISSN 0093 0415

1999 SUBSCRIPTION RATES

- ☐ Individual rate: $70 US/Canada; $85 Outside US/Canada
- ☐ Institutional rate: $120 US/Canada; $130 Outside US/Canada
- ☐ Start Issue..... (month/year)
- ☐ Send me Guidelines for Authors

My primary speciality is.....

Years in practice .....

- ☐ I enclose a check for $..... (Payable to Western Journal of Medicine)

US Dollar checks to be drawn on a US bank account.

...../...../...../.....

AMEX/Visa/Mastercard/ (delete as appropriate)

Expiration date .....

Signature ..... Date .....

(Your signature is essential when paying by credit card)

Name .....

Address .....

(Please print your billing address)

.....

.....

City .....

State, Zipcode .....

Return to:

WJM, PO Box 590A, Kennebunkport, ME 04046,
Phone: 1-800-236-6265 Fax: 1-800-232-9265
Email: bjpaige@cybertours.com

WJM Western Journal of Medicine

Publication: Monthly ISSN 0093 0415

1999 SUBSCRIPTION RATES

- ☐ Individual rate: $70 US/Canada; $85 Outside US/Canada
- ☐ Institutional rate: $120 US/Canada; $130 Outside US/Canada
- ☐ Start Issue..... (month/year)
- ☐ Send me Guidelines for Authors

My primary speciality is.....

Years in practice .....

- ☐ I enclose a check for $..... (Payable to Western Journal of Medicine)

US Dollar checks to be drawn on a US bank account.

...../...../...../.....

AMEX/Visa/Mastercard/ (delete as appropriate)

Expiration date .....

Signature ..... Date .....

Name .....

Address .....

(Please print your billing address)

.....

.....

City .....

State, Zipcode .....

Return to:

WJM, PO Box 590A, Kennebunkport, ME 04046,
Phone: 1-800-236-6265 Fax: 1-800-232-9265

IF MAILED
IN THE
UNITED STATES

BUSINESS REPLY MAIL
FIRST-CLASS MAIL PERMIT NO. 26755

POSTAGE WILL BE PAID BY ADDRESSEE

WJM Western Journal of Medicine
P.O. BOX 590A
KENNEBUNKPORT, ME 04046

NO POSTAGE
NECESSARY
IF MAILED
IN THE
UNITED STATES

BUSINESS REPLY MAIL
FIRST-CLASS MAIL PERMIT NO. 26755

POSTAGE WILL BE PAID BY ADDRESSEE

WJM Western Journal of Medicine
P.O. BOX 590A
KENNEBUNKPORT, ME 04046

NO POSTAGE
NECESSARY
IF MAILED
IN THE
UNITED STATES

BUSINESS REPLY MAIL
FIRST-CLASS MAIL PERMIT NO. 26755

POSTAGE WILL BE PAID BY ADDRESSEE

WJM Western Journal of Medicine
P.O. BOX 590A
KENNEBUNKPORT, ME 04046

Recent developments in medical care of Jehovah's Witnesses

see also p.307

Osamu Muramoto

Regional Ethics Council and Department of Neurology, Kaiser Permanente Northwest Division, and Northwest Permanente P.C., Portland, Oregon

Correspondence to:
Dr Muramato
Kaiser East Interstate Office, 3414 N.W. Kaiser Center Drive, Portland, OR 97227
muramotosa@kpnw.org

Summary Points

- Despite progress in bloodless medicine, the care of Jehovah's Witness patients who refuse blood-based treatments is difficult .
- An agreement signed by the organization at the European Commission of Human Rights states that Jehovah's Witnesses should have free choice to receive blood transfusions without any control or sanction from the organization.
- The recent emergence of reform Jehovah's Witnesses, who petition for a right to freedom of personal choice to accept or refuse blood transfusions, indicates a growing diversity among the followers in their attitudes toward the blood policy.
- An individualized approach to each patient, respecting their diversity of beliefs and values, has become increasingly important.

Introduction

Since 1945, the Watchtower Bible and Tract Society (WTS), the controlling religious organization of Jehovah's Witnesses (JWs), has promulgated to all its followers a doctrine to refuse blood and certain blood products for their medical treatment. They teach that the biblical command, "you must not eat blood" (Leviticus 17:12) and "abstain from blood" (Acts 15:29), means "not taking it into our bodies at all," including prohibition of the medical use of blood.[1] For the past half century, this doctrine has brought numerous challenges in medical care of JW patients, and occasionally tragic premature deaths. Although the doctrine is said to be an "everlasting law" of God, it has recently undergone major revisions. In this review, I will discuss some of these developments, which impact on the medical care of approximately ten-million adherents world-wide for whom blood treatment may be an issue.

Distinction between acceptable and unacceptable treatments

For physicians who treat JWs, one of the most puzzling aspects is that they are, in fact, accepting many blood-based treatments despite their belief in absolute abstinence from blood. Since this biblical law is said to be absolute, it is unclear why the WTS does not teach its members to simply refuse all medical use of blood. On one hand, they teach that God prohibits any intake of blood into the body regardless of the methods, whether eating it in the biblical era, or infusing it in modern medicine. On the other hand, they have meticulously sorted out various methods of blood intake in medical settings, and classified them either as acceptable or unacceptable, depending on the method. As new blood-based treatments become available, such classification has become a daunting task.

Table 1 summarizes the current policy and practice of prohibited and acceptable treatments. Table 2 shows the complex conditions under which the same or similar material or procedure may become acceptable or unacceptable. Information in these tables is a composite from WTS publications, including their advance directive form, as well as articles by JW physicians.[2,6] Many JWs do not understand or remember such complicated regulations.

Table 1 *Current policy and practice of WTS on prohibited and acceptable treatments*

Prohibited Blood Components and Procedures	Acceptable Blood Components and Procedures
• Whole blood	• Plasma proteins (albumin, globulin, fibrin)
• Red blood cells	• Clotting factors
• Platelets	• Stem cells
• Plasma	• Hemodilution, cell saver
• Hemoglobin solution	• Bone marrow transplants
• Stored autologous blood	• Extracorporeal circulation (heart-lung machine, dialysis, plasmapheresis)
• Blood donation	• Use of donated blood (to take acceptable components)

Abbreviations used in text: JW=Jehovah's Witness, WTS=Watchtower Bible and Tract Society; HIS=Hospital Information Service; HLC=Hospital Liaison Committee; AJWRB=Associated Jehovah's Witnesses for Reform on Blood .

These facts have prompted the WTS to form the "Hospital Information Service" (HIS) in its headquarters, a public relations office for the blood policy. It answers inquiries regarding "no-blood" treatment, and interprets the rules and conditions for patients and doctors. The HIS researches medical literature, recommends various no-blood treatments, and provides references to cooperative physicians. In addition, more than 1200 "Hospital Liaison Committees"(HLCs), which consist of selected elders who received special training from HIS, are established worldwide. Its members visit hospitals to present the policy. They provide the same service as HIS locally, and can intervene between JW patients and physicians as needed.

Reform movement inside JWs

Since 1996, a growing number of JWs, including some members of HLCs, have expressed anonymously their dissent to the blood policy.[10] They formed a group called the Associated Jehovah's Witnesses for Reform on Blood (AJWRB).[11, 12] They call for a reform of the blood policy which, according to them, is plagued by a complicated web of contradictory rules and conditions strictly enforced without biblical basis. Some members of HLCs have resigned because of what they call "Pharisaic" rules. The WTS has dismissed them as "disaffected ones" and discredited them because of AJWRB's anonymity.[13, 14] However, according to AJWRB, it is not possible, other than anonymously, for a JW to voice any criticism of the WTS or propose any reform from within the organization, because such public expression almost certainly results in expulsion of the members.[12]

The significance of this reform movement for physicians is awareness of a growing diversity of values and beliefs among individual JWs, who have long been viewed as a uniform religious group. Such diversity requires physicians to scrutinize the patient's premolded medical directive more closely and take a more individualized approach.

Freedom of choice in JWs' medical care

Although it is well known that the WTS has fought many years for freedom of choice to refuse blood transfusions vis-á-vis legal authorities and medical professions—members within the WTS are not accorded the same freedom of choice to receive blood transfusions without penalty. The fact that the very freedom that the WTS has demanded outside the organization has been denied inside the organization is another major point of reform called for by the AJWRB. Any JW who openly and willfully receives a

Table 2 *Complex conditions that make similar components/procedures acceptable or unacceptable*

	JWs May Not Accept	JWs May Accept ....
Whole blood[2]	IF taken as "blood transfusion" #	IF taken as contained in bone marrow transplants[3]
Plasma proteins[2]	IF taken together as "plasma" #	IF taken separately as individual blood component (albumin, globulin, clotting factors, fibrin)
White blood cells[2]	IF taken as "white blood cells" #	IF taken as "peripheral stem cells"[4, 5]
Autologous blood[2]	IF tube connection to the patient's body is interrupted #	IF tube connection to the patient's body is maintained (hemodilution, cell saver)
	IF it is stored #	IF taken as "peripheral stem cells" (even if it is stored)[4]
Stem cells[6]	IF taken from umbilical cord blood[7]	IF taken from peripheral blood or bone marrow[3, 4]
Major protein from prohibited component	IF taken from red blood cells (hemoglobin)[6] #	IF taken from plasma (albumin)[2]
Heart-lung machine[2]	IF patient's blood is used to prime the machine #	IF patient's blood is used to circulate in the machine
Epidural blood patch[8]	IF blood is removed from vein and injected	IF injecting syringe is connected to vein via tube
Blood donation[9]	IF donated by JWs for use of JWs and others #	IF donated by non-JWs for use of JWs and others

Conditions marked by # are observed by JWs without exception. Other conditions are observed by many JWs but with exceptions. For example, JWs never accept a heart-lung machine primed with blood, but most, if not all, JWs accept the machine as long as it is circulated with own blood.

prohibited blood-based treatment and does not repent of the action before a "judicial committee" will receive the harshest sanction of the religion, excommunication or "disfellowshipping." This is considered equal to betraying God and involves shunning, or isolation from normal association or fellowship with family and life-long friends who are members. Many former JWs testify to the psychological trauma associated with leaving the religion.

This punitive measure may soon change. One of the most important developments of the blood policy of JWs in recent years is the public agreement established in 1998 between the WTS and the government of Bulgaria at the European Commission of Human Rights. The WTS agreed that JWs in Bulgaria "should have free choice" to receive blood transfusions "without any control or sanction on the part of the association."[15, 16] This apparent compromise was made in exchange for registration of JWs as a religion in that country. The WTS has been reticent with their members about their promise of "free choice" in Bulgaria, and only issued a letter and a press release stating that there has been no change in the blood policy.[16a] Nevertheless, a WTS representative, quoting the charter accepted by the Bulgarian government, now states that the WTS "may not exercise control over free will of believers but allows them to exercise their conscience consistent with godly Bible principles." He also states that the WTS does not "arbitrarily apply sanctions in connection with the medical care that Jehovah's Witnesses conscientiously seek for themselves and children," and this, according to him, is the established beliefs of JWs internationally.[14]

These statements appear to conflict with the enforced policy of expelling and ostracizing those who conscientiously receive blood transfusions and do not repent. According to AJWRB, these WTS statements could be interpreted to mean that each member may exercise personal conscience to choose which blood components are acceptable in medical treatment, since the "godly Bible principles" are silent over what is or is not acceptable in blood components. On the other hand, the statements allow the WTS to "non-arbitrarily apply sanctions" and to continue to "exercise control over free will." We should expect further clarification from the WTS to explain this discrepancy. In the meantime, it is an indication that JWs may soon be given the right to choose their own medical care, including acceptance or refusal of blood, without organizational control.

Ethical and legal issues of the blood card and informed refusal

The use of the "blood card," a wallet-sized advance directive created by the WTS and carried by JWs, has been controversial. The card is intended to document the JW's informed refusal of blood in the event of an emergency. Yet, the validity of the card has been questioned, particularly when a JW patient presents to the emergency room unconscious and exsanguinating, with the blood card being the only expression of will.[17] There are two main reasons to challenge the validity of such cards.

First, it is unclear whether such a directive was signed as a spontaneous and personal decision, or as an obligation to comply with the organizational rules as a member. Every year in January, new cards are handed out to all JWs to sign. Group leaders are instructed to ensure that every member sign the card during a private group meeting. Such a signing procedure could be coercive due to strong peer pressure.

Catheryn Proctor, right, mother of Jadine Russell, a pedestrian who died after being hit by a drunk driver, wipes away a tear outside the courtroom after the driver's trial. The victim, a Jehovah's Witness, refused a blood transfusion, which the defense argued actually caused her death. *Victoria Arocho/ Associated Press.*

Second, there is a serious concern whether JWs were adequately informed of the risk versus benefit analysis of blood-based treatments when they signed the card. In their official magazines, horrifying stories about tragic cases of blood-based treatments collected from medical journals and news media have been presented, yet there has never been any article that objectively weighs the benefit of blood transfusions against the risk. Such biased information raises serious concern about the validity of the informed refusal expressed in the blood card.

As Migden and Braen stated,[17] it appears that the real purpose of the blood card is not to ensure that JWs make an informed decision regarding blood-based treatment, but rather to prevent JWs from receiving blood. Under such strict organizational directives imposed by the WTS, autonomy of JW patients, which is a prerequisite

of informed consent, may be suppressed. Considering these factors, Migden and Braen concluded that a good faith decision to transfuse an unconscious adult JW in emergent need of blood is justified if the patient does not have a blood refusal advance directive that is informed and can survive a high level of scrutiny.

In view of such potential problems of the blood card, the WTS in recent years has put more emphasis on filling out a full advance directive form for refusal of blood, in conjunction with a health-care power of attorney (proxy) form prepared by the WTS for each state. JWs are encouraged to fill out these forms and submit them for their health care providers to have on record. The forms include legal references for judges and hospital lawyers who may question or challenge the legality of the blood policy. The forms detail WTS-approved alternatives for blood treatment, and instruct as to what treatments JWs must not accept under any circumstances, even to save their lives. The forms also list which blood components and procedures may be allowed and under what circumstances, subject to an individual's conscience (see Table 1 and 2). The WTS now encourages JWs to indicate on the blood card that they have executed the advance directive forms of their state.

Clinical management of JW patients

When no life-threatening condition exists, and alternative bloodless treatment is readily available without excessive cost or risk, treatment of JWs should be no different from other patients. They do not refuse other medical treatment and are generally conscientious about their own health and respectful of physicians.

Major ethical controversy arises when there are limited or no alternatives to blood-based treatment. Until the WTS publishes more simplified rules, and allows all medical treatment decisions to be based on individual conscience, the care of such JW cases will remain complicated. It is not sufficent to either blindly comply with the pre-molded directive, or flatly refuse treatment and refer to another hospital or doctor.

The patient's personal beliefs and understanding of the risk versus benefit should be carefully discussed in private conference. Religious discussion need not be avoided since organizational control of patients' choices are inseparable from their religious conviction.[18] Only a small number of JWs understand the complex rules and conditions of blood policy of their own organization. For this reason, I recommend that any medical professionals dealing with JW patients obtain a small brochure *Do Jehovah's Witnesses Really Abstain From Blood?* published by AJWRB [19] for reference in such discussions. It is written by JWs themselves and concisely discusses the questions of the blood policy. It is also important to seek ethics consultation in complicated cases.

What is acceptable or unacceptable treatment should ultimately be determined by the individual patient, in concert with advice from treating physicians. Some JW patients may delegate their decision to the WTS and ask the H.L.C to intervene on their behalf. Others may be autonomous enough to make individualized decisions based on new perspectives.

Whatever decision the patient makes, extra precaution must be taken to ensure the privacy and confidentiality of those decisions. The WTS once published an article in its official magazine that encouraged JWs who work in the medical field to divulge confidential medical information of fellow JW patients who secretly receive medical treatment prohibited by the WTS.[20]

Life-threatening emergency treatment of exsanguinating JW patients continues to be problematic. There is no time to obtain informed consent to transfuse blood. Every effort should be made to stabilize the patient so that valid and contemporaneous informed consent can be obtained. If the patient is unable to express a contemporaneous decision and there is no valid advance directive, or there is reasonable doubt about the validity of the blood card, emergency blood transfusions may be given until the patient is relieved from imminent danger of death.[17]

There are several reasons to support this course of action. First, emergency exception to consent has been an established medicolegal principle. The Pennsylvania Supreme Court held that "...where there is an emergency calling for an immediate decision, nothing less than a fully conscious contemporaneous decision by the patient will be sufficient to override evidence of medical necessity."[21] Second, JWs who were unconsciously transfused are not subject to the religion's judicial process or sanctions. Third, as reviewed here, since there is an indication of change in the policy on the horizon, premature death at the present time due to blood loss must be averted.

Treatment of children

Children of JW parents should be given treatment independently from their parents' religion. As the Committee of Bioethics of the American Academy of Pediatrics stated, "constitutional guarantees of freedom of religion do not permit children to be harmed through religious practices."[22] In emergency situations where there is risk of harm to the child by withholding blood-based treatment, immediate danger should be relieved, including, if necessary, giving blood-based treatment. Decisions regarding "mature minors" or adolescent children are more problematic. The maturity of each child is different, and so is the child's understanding and commitment to the blood policy. If there is any unsolved ethical or legal issue regarding JW children, it is most appropriate to obtain a court order before proceeding further.

Disclaimer/Disclosure Views and opinions expressed herein are the author's and do not necessarily reflect those of Kaiser Permanente and Northwest Permanente P.C. The author has served as a medical consultant to the AJWRB since 1997 without compensation. He has never been a Jehovah's Witness.

Sources and References

1. *You Can Live Forever in Paradise on Earth.* Brooklyn: Watch Tower Bible and Tract Society of Pennsylvania, 1989, p216.
2. Dixon JL, Smalley MG. Jehovah's Witnesses. The surgical/ethical challenge. *JAMA* 1981; 246:2471-2472.
3. Questions from readers. *The Watchtower;* 1984 May 15:31.
4. Kerridge I, Lowe M, Seldon M, Enno A, Deveridge S. Clinical and ethical issues in the treatment of a Jehovah's Witness with acute myeloblastic leukemia. *Arch Intern Med* 1998; 157:1753-1757.
5. Muramoto O. Medical ethics in the treatment of Jehovah's Witnesses. *Arch Intern Med* 1998; 158:1155-1156.
6. Malak J Jehovah's Witnesses and medicine: an overview of beliefs and issues in their care. *J Med Assoc Ga* 1998; 87:322-327.
7. Questions from readers. *The Watchtower*, 1997 Feb 1:29.
8. Kanumilli V, Kaza R, Johnson C, Nowacki. Epidural blood patch for Jehovah's Witness patient. *Anesth Analg* 1993; 77:872-873.
9. Questions from readers. *The Watchtower*, 1961 Jan 15:64.
10. Muramoto O. Bioethics of the refusal of blood by Jehovah's Witnesses: Part 1. Should bioethical deliberation consider dissidents' views? *J Med Ethics* 1998; 24:223-230.
11. "New Light on Blood. Official site of The Associated Jehovah's Witnesses for Reform on Blood:" http://www.visiworld.com/starter/newlight/index.htm.
12. The Liberal Elder. Reply to Malyon on respecting the autonomy and motives of Jehovah's Witness patients. *J Med Ethics* (Submitted for publication).
13. Malyon D. Transfusion-free treatment of Jehovah's Witnesses: respecting the autonomous patient's rights. *J Med Ethics* 1998; 24:302-307.
14. Malyon D. Transfusion-free treatment of Jehovah's Witnesses: respecting the autonomous patient's motives. *J Med Ethics* 1998; 24:376-381.
15. Communique issued by the Secretary to the European Commission of Human Rights. INFORMATION NOTE No. 148 on the 276th Session of the European Commission of Human Rights. (Strasbourg, Monday 2 March-Friday 13 March 1998). http://194.250.50.201/eng/E276INFO.148.html.
16. Muramoto O. Jehovah's Witnesses and blood transfusions. *Lancet* 1998; 352:824.

16a. Wilcox P. Jehovah's Witnesses and blood transfusions. *Lancet* 1999; 353:757-758.

17. Migden DR, Braen GR. The Jehovah's Witness blood refusal card: ethical and medicolegal considerations for emergency physicians. *Acad Emerg Med* 1998; 5:815-824.
18. Muramoto O. Bioethics of the refusal of blood by Jehovah's Witnesses: Part 2. A novel approach based on rational non-interventional paternalism. *J Med Ethics* 1998; 24:295-301.
19. Do Jehovah's Witnesses really abstain from blood? Boise: The Associated Jehovah's Witnesses for Reform on Blood. 1998 (available by writing to AJWRB, PO Box 190089 Boise, ID 83719-0089, or online at http://www.visiworld.com/starter/newlight/doctor.htm).
20. "A time to speak"—when? *The Watchtower*, 1987 Sept 1:12.
21. Re Estate of Darrell Dorne, 534 A.2d 452 (Pa. 1987).
22. American Academy of Pediatrics Committee on Bioethics. Religious objections to medical care. *Pediatrics* 1997; 99:279-281.

CDrom REVIEW

The Cochrane Library 1998 Issue 4
Update software, updated quarterly; ISBN 0 72279 1089 2

Rating: ★ ★ ★ ★
Price: $225

Illness and its treatment are often transforming experiences. It follows that decisions about treatment can be fateful for patients. Such decisions ought to be informed by the best evidence regarding the effectiveness of available interventions. However, timely access to the best evidence is elusive. It requires an organizational and analytical enterprise so prodigious that, until now, it has been beyond the grasp of individual clinicians and the profession as a whole. The Cochrane Library represents a formidable attempt to provide a response worthy of the vision of effective and efficient health care articulated decades ago by the project's namesake, the late A. L. Cochrane. He would be proud of the library that carries his name.

The Cochrane Library consists of (1) the Cochrane Database of Systematic Reviews, currently containing 438 protocols for reviews, including many that address problems commonly seen in general practice; (2) the Database of Abstracts of Reviews of Effectiveness, containing nearly 2000 abstracts of evidence based reviews, some with commentaries about their quality; (3) the Cochrane Controlled Trials Register, with more than 200,000 trials listed; and (4) the Cochrane Review Methodology Database, with 836 citations and abstracts that address methods for unbiased collection and interpretation of evidence. For most users, the completed systematic reviews will be most valuable.

Because medicine's knowledge base is constantly expanding, any useful compendium must be cumulative. This is the fourth issue of 1998, and revised issues are published quarterly. But the library is a work in progress in other ways. Updating is uneven. The coverage of different conditions and of various treatments for the same condition varies. The level of detail is more likely to reflect the interests of those committed to the enterprise than the burden of illness conferred by a condition or other measures of priority. For example, about a third of the completed reviews address evidence regarding care related to pregnancy and childbirth.

The formats used to present and catalogue reviews reflect more the mindset of a researcher or a librarian than that of a user—doctor; patient, or policy maker—trying to make an evidence based decision. But the search and display functions are well designed and easy to learn. The library will not always inform decisions, however, even if relevant reviews have been completed. It is, after all, a compendium of available evidence, and much of what needs to be known to make a good decision has not been well studied. Moreover, good clinical decisions will often depend on preferences for possible outcomes and attitudes toward risks, which will vary considerably among users of evidence.

These are quibbles, and one would expect these limitations of a work in progress produced by a collaboration convened across national and disciplinary boundaries and sustained by a common view of professional responsibility. Furthermore, to cite limitations of The Cochrane Library begs a comparison, and there is none to make. Use today's library despite its gaps. Better yet, find a way to help the Cochrane Collaboration make tomorrow's physicians and patients realize the promise of effectiveness and efficiency in heath care.

—Albert C. Mulley, *Associate Professor of Medicine*, Harvard Medical School, Boston, Massachusetts, USA

In the Public Eye

Media Watch

Deborah Josefson, Physician and Journalist, San Francisco, CA
Debdoc.@aol.com

In late 1997, Sharon Bernstein, a 35-year-old *Los Angeles Times* journalist and a new mother, was assigned the county hospital beat. Recently pregnant, the reporter was drawn towards stories of maternal and fetal health. So, she decided to look into obstetric malpractice claims against county hospitals. What she uncovered would change county hospital policy, lead to an assembly bill, and rekindle the medical debate about the safety of lowering Caesarean section (C-section) rates.

In a series of recent articles in the *Los Angeles Times,* Bernstein exposed a systematic policy at University of Southern California-Los Angeles (USC-LA) County hospitals from the mid-1980's to 1995, which mandated a trial of labor (TOL) prior to C-section for all women regardless of risk. During this time period, large increases in birth complications were noted. So many occurred that the hospitals abandoned their own policy in 1995 after an internal review. In a 5-year period alone, 53 birth injury lawsuits were filed and the county paid out $24 million to settle 49 claims of mothers and children who suffered when doctors insisted that women attempt to deliver vaginally. The complications included the deaths of 2 mothers and 3 infants, 2 uterine ruptures, 10 brachial plexus injuries, 5 cases of cerebral palsy, and 15 cases of learning disabilities deemed secondary to anoxia during prolonged labor. Because the hospitals were public city hospitals serving mainly the urban poor, concern was raised that the practice was discriminatory and financially motivated. After all, many of the patients were immigrants who lacked medical insurance, and the cost of Caesarean deliveries is about twice that of vaginal deliveries.

But the story is more complicated. City hospital overcrowding was rampant during this time, and it was impossible to run enough operative suites for more than a few simultaneous C-sections. This alone would lead doctors to proceed with a trial of labor. Additionally, although the clientele at county hospitals was mostly poor, the trial of labor policy held for affluent patients as well.

Significantly, the hospitals were at the forefront of a national movement, formed by natural childbirth advocates, midwives, and lobbies of health maintenance organizations (HMOs) as well as the federal government, to reduce the number of Caesarean sections. In fact, the rate of vaginal births and vaginal births after Cesarean section (VBACS) are used as quality indicators for many HMOs and for the accreditation of hospitals. In any case, Bernstein's articles led to a re-examination and ultimately a 180 degree reversal of county hospital policies, and the passage of an assembly bill to track obstetric complications and malpractice suits. Now patients at USC-LA County hospitals who have had a prior C-section must sign a consent for a vaginal birth.

Caesarean sections can be safer. *John Smith/Custom Medical Stock/Science Photo Library*

"Once a C-section, always a C-section," a self-perpetuating cycle is initiated as repeat C-sections account for as many as 30% of all surgical births.

In the United States, C-sections increased fivefold, from 5% in the late 1960s, to 25% by the 1990s. (*American Journal of Obstetrics and Gynecology,* 176:741-4). Although the etiology of the current C-section epidemic is complex, prime contributive factors include the advent of fetal monitoring, fear of malpractice litigation, epidural anesthesia, and physician and patient preference. Additionally, following the outmoded dictum "Once a C-section, always a C-section," a self-perpetuating cycle is initiated as repeat C-sections account for as many as 30% of all surgical births.

In 1995, when the nationwide C-section rate reached up to 50% at some private hospitals and 21% nationwide, the Department of Health and Human Services (DHHS) announced its goal of reducing C-sections to 15% of all births by 2000. Los Angeles County Hospitals had already reduced the number of C-section births to 10% by 1989. This was achieved largely through the policy of a mandatory trial of labor in concert with instrumental vaginal deliveries. Such policies were not unique to LA county, and many private institutions sought to decrease C-section deliveries through identical strategies as well as peer review pressure. (*American Journal of Obstetrics and Gynecology,* 178:1207-14).

TOL are usually stopped when fetal distress or failure to progress is diagnosed. In busy urban hospitals such as those in Los Angeles, delays in making these diagnoses were possible. There are few absolute contraindications to a TOL, but most physicians agree that a prior classical vertical Caesarean incision, a history of uterine rupture or dehiscence and persistent cephalopelvic disproportion are among them. It is unclear if any of the lawsuits against LA county hospitals involved these absolute contraindications.

Relative contraindications for a TOL include two or more previous C-sections and multiparity. Instrumental vaginal deliveries also have complications, as the incidence of brachial plexus injuries and cephalohematomas are increased with forceps and vacuum deliveries.

The American College of Gynecology recommends a trial of labor for nearly all births, and notes that most women who have had prior transverse abdominal C-sections can successfully deliver vaginally thereafter.

A *NEJM* editorial earlier this year, however, says that reducing the C-section rate to 15% may adversely affect maternal and infant health. It argues that there is no evidence for this target rate, and that such an arbitrary policy limits women's say in their health care. Interestingly, the same article mentions the *LA Times* pieces, but concludes that most of the bad outcomes listed can't be attributed to a previously scarred uterus.

A new consensus against severe C-section reductions may be emerging. Commenting on the DHHS goal to reduce Caesareans, Dr. Bruce Flamm of Kaiser Permanente, Southern California, a national expert on reducing surgical births through VBACs said: "There's no question that it can be done. The question is can it be done safely and should you do it? Our system has a 24-hour in-house obstetrics-gynecology, anesthesia and nursing team and our outcomes are good even in the case of uterine rupture. Whether these results can be replicated nationwide and at rural and urban hospitals is doubtful."

Dr. Flamm added: "What I've found out going to meetings is that the VBAC rate has fallen dramatically in the past few years partly as a result of the media attention from the USC (University of Southern California-county hospitals) experience, but also because in late 1996, a VBAC consent form was developed by Dr. Jeff Phelan, an obstetrician and attorney. The consent asks women who want to undergo a VBAC to sign a consent form warning of the risks, including that of uterine rupture, permanent injury and fetal brain damage. Kaiser has a similar consent form." And now, due to media pressure, patients at county hospitals also have a choice.

News and Features

New malaria vaccine shows promise

Deborah Josefson, *San Francisco*

An experimental malaria vaccine designed to protect the host from each stage of the parasite's life cycle has shown promise in animal trials (*Proceedings of the National Academy of Sciences* 1999; 96:161520).

Researchers from the US Centers for Disease Control and Prevention in Atlanta, Georgia, have created a recombinant, multivalent vaccine against *Plasmodium falciparum,* the deadliest malaria parasite. This vaccine differs from previous vaccines because it contains multiple antigens and targets the parasite at several stages in its life cycle.

Malaria infects about 400 million people a year and kills 3 million annually. About one third of the world's population is at risk of infection. Although public health measures and antimalaria drugs such as choloroquine have been somewhat successful in containing the parasite, chemoresistant strains have emerged in recent years. The development of an effective malaria vaccine has become an international health priority.

Construction of a successful vaccine has been hampered by the complexity of the parasite's life cycle. In addition to both the mosquito vector and vertebrate phases, the parasite undergoes multiple incarnations within its host. For instance, it has an asexual sporozoite phase in which it freely circulates within the bloodstream, a gametocytic phase within red blood cells, a schizont phase, and a merozoite phase within hepatocytes. The parasite's identity changes through each of these stages including changes in surface antigens and this presents a challenge to vaccine development.

Additionally, the parasite cloaks itself in different proteins during the erythrocytic and hepatocytic phases, and these membrane proteins also undergo phenotypic variation. Therefore a vaccine directed against a single epitope or which targets only one phase of the parasite's life cycle may not be sufficient to induce protective antibodies.

The centers scientists, led by Altaf Lal, took advantage of the parasite's complicated life stages by constructing a vaccine which combined segments of 21 different *P falciparum* peptides into a single recombinant protein. The peptides were selected because each of them had been shown to be immunogenic in previous vaccine trials.

Different parts of the hosts immune system B cells, helper T cells, and cytotoxic T cells were activated by the peptides. The vaccine was injected into rabbits. Laboratory tests showed that the vaccine was successful in inducing antibodies to various stages of *P falciparum's* life cycle, inhibited its growth and replication in red cells, and prevented the parasite from entering liver cells.

The scientists plan to test the vaccine on nonhuman primates before proceeding to human trials. Commenting on the study, Dr Anthony Fauci, director the National Institute of Allergy and Infectious Disease said: "Although these results are preliminary and the candidate vaccine has yet to be tested in people, its effectiveness in laboratory tests makes it an interesting candidate for further study."

Epidural analgesia must be paid for in cash in advance

James Ciment, *New York*

Responding to reports that certain hospitals are requiring patients with Medicaid undergoing childbirth to pay for epidural analgesia in cash and in advance, the director of the Center for Medicaid and State Operations, an agency within the US Department of Health and Human Services, issued a letter to state Medicaid directors across the country reminding them of their responsibilities and demanding that action be taken.

Last year, more than 1 out of 3 childbirths in the country were paid for by Medicaid. In epidural analgesia, local anesthetics are delivered in to the epidural space for pain relief in labor. In her letter of January 27, director Sally Richardson wrote, "Treatment of a Medicaid patient in this manner is not just a concern, it is alarming.... A hospital which accepts a Medicaid patient for treatment accepts the responsibility for making sure that the patient receives all medically necessary services."

The incidents that sparked the warning letter occurred in New York, although the national Medicaid office acknowledged that they have heard similar stories from California as well. One case cited in the letter concerned a woman in New York City whose obstetrician had ordered the epidural analgesia in advance. But while in labor, the woman was refused the service because she had not prepaid in cash, despite the fact that she offered a check, a Western Union money telegram, and a credit card to pay for the analgesia.

Mary Kahn, a spokeswoman for Medicaid, said that these incidents hint at a much larger problem. "It worries us that this is going on all over the place, but that the patients are not reporting it. And if they are not reporting it, we don't know it is happening." Referring to the Medicaid patients generally, she added: "We hope that these stories will stir up people to let us know."

FDA proposes testing animal feed antibiotics

James Ciment, *New York*

The problem of antibiotic-resistant bacterial strains in the American food supply has once again come under scrutiny from the Food and Drug Administration. In the past few weeks, the agency has proposed a plan to test and report on the quantity and human health implications of antibiotics routinely added to animal feed.

Opponents of feed antibiotics say that their use increases the likelihood of the development of pathogens resistant to antibiotics. In early March, a coalition of 41 health and consumer groups requested that the FDA ban the routine use of antibiotics in feed if those same drugs were used for humans. A similar ban has been in effect in the European Union since last year, imposed in the wake of the outbreak of "mad cow" disease in Britain.

Both the request for the ban and the FDA proposal come in the wake of an article published last year in the *New England Journal of Medicine,* which noted the emergence of a superstrain of food borne salmonella resistant to most drug treatments (1998; 338).

Virtually unknown a decade ago, this multidrug resistance threatens the recovery of millions of people struck by the disease annually. It is estimated that farmers mix up to 7.3m kg of antibiotics into the feed and water of chickens, pigs, and cattle annually, accounting for nearly one third of all antibiotics used in the country.

American trade union aims to recruit more doctors

Fred Charatan, *Florida*

Service Employees International Union, the largest healthcare union in the United States, has pledged $1 million in its drive to recruit salaried doctors, about half of the 600,000 practicing doctors in the United States. About 35,000 doctors (6%) are already unionized.

The union plans to focus on the states of California, Florida, and Washington, as well as the District of Columbia, where doctors' unions are relatively strong. Doctors began to join unions in the 1970s, motivated by a revolution in health care.

The rush to join unions came because "American health care is in a state of hyperturbulence characterized by accumulated waves of change in payment systems, delivery systems, technology, professional relationships, and societal expectations," according to Professor Grace Budrys, the author of *When Doctors Join Unions,* (Cornell University Press, 1997, p.2).

"I can see the time coming when we're not simply independent business owners...but just workers," said Dr Lawrence Koning, an obstetrician and gynecologist who is a member of the Union of American Physicians and Dentists in Oakland, California.

"Doctors are being fired, they're being cut back, they're being told what to do or how much to make...We have no power."

The American Medical Association (AMA), while strongly in favor of doctors engaging in collective bargaining with employers such as health maintenance organizations and managed care companies is against doctors joining unions. The AMA sees a conflict of interest between a doctor's professional identity and trade unions' use of strikes as the ultimate weapon.

Doctors belonging to a union would be expected not to cross picket lines, for example, if other union members such as nurses went on strike. This would result in a clear ethical dilemma for doctors.

Federal law also bars doctors from joining unions because they are viewed primarily as independent contractors

News in brief

Physicians worry about reporting domestic violence cases to police

The majority of California physicians worry that patient confidentiality could be destroyed by mandatory reporting of domestic violence to police, says a study in the American Journal of Public Health last month. The study, from UCSF, randomly surveyed 508 Californian physicians, from emergency medicine, family medicine, internal medicine and obstetrics/gynecology. Nearly 60% said they might not comply with the law if a patient objected. Most also believed that reporting could lead to worse domestic violence. California, along with New Mexico, Colorado, Kentucky, New Hampshire and Rhode Island, has specific laws requiring physicians to contact police with suspicion of partner violence. "The findings support the concern that this law violates basic tenets of medical ethics and may create barriers to health care for victims," warns study director Michael Rodriguez, assistant professor of family and community medicine at UCSF.

Routine vaccination against Hepatitis A recommended by CDC

Routine vaccination against Hepatitis A for some US children has been recommended by the Centers for Disease Control. In 14 states where rates of infection are higher than 20 per 100,000 persons, the CDC advises that vaccination, which costs about $50 a child, is cost effective. About 60 000 children under the age of 15 years get the disease each year. So far, New Mexico has responded to the CDC saying that it will continue its policy of vaccinating in "hot spots" only.

Futile care policies should be backed by fair process says AMA *see also p.287*

When patients or their loved ones disagree with physicians over how much further care the patient should be given, the health care institution should have processes in place to resolve disputes. The AMA's Council on Ethical and Judicial Affairs recommends prior discussion between patients, relatives, and physicians over what care would be considered futile and joint decision making using outcome data. In nonresolvable cases, the ethics committee should get involved. If agreement still cannot be reached, alternative care within the institution, or in another hospital, should be arranged. If this is not possible, the futile treatment should stop, says the Council.

in private practice. Under antitrust laws, doctors cannot join together to set terms of remuneration.

"The balance of power in the marketplace has tilted so far toward insurers and their shareholders and away from the interests of our patients, that it has placed our patients and their physicians in a very dangerous position," said Dr Randolph Smoak, the chairman of the AMA board of trustees.

The AMA supports a bill, the Health Care Coalition Act, to be introduced in Congress by California representative Tom Campbell, which would grant collective bargaining rights to healthcare professionals negotiating terms of employment with health maintenance organizations.

Fat people offended by West Coast gym advertisements

Scott Gottlieb, *New York*

Ben Margot/Associated Press.

A new billboard for a 24-hour fitness center in San Francisco that depicts aliens and reads, "When they come, they'll eat the fat ones first," is creating a stir over what is acceptable advertising, and what sensitivity is owed to those who are fat.

The month-old billboard has infuriated a group of self-described fat activists, who came out recently to protest the ad and the antifat ethos they say is prevalent in many gyms.

"I find the ad very offensive," said Francis White, director of the National Association to Advance Fat Acceptance. "The billboard never would have seen the light of day if any other group in this society was targeted. Fat people are the last safe prejudice," she said.

People of weight responded with equally humorous protests. They conducted an aerobics class in front of the health-club chain's outlets and waved signs reading "Eat Me," "I'm Yummy," and "Bite My Fat Alien Butt."

"It's a serious issue," said Marilyn Wann, author of the book *Fat? So*, who organized the protests of the billboard advertisement. "I encourage people of all sizes to exercise. But I think this ad isn't helping much, and the whole fitness industry isn't really helping much, because gyms are pretty intimidating places," Wann said.

Despite the protests from fat activists, the health club said it has no plans to change its advertisement.

"As we know, obesity is one of the leading causes of health care costs in our society. It's no laughing matter at all," said Craig Pepin-Donat, northwest division president of 24 Hour Fitness, the chain of 284 gyms based in San Diego County that ran the ad. The company said there was no intention to offend anyone with its current ad.

"This country is the fattest nation in the world today," said Mark Mastrov, chief executive officer of 24 Hour Fitness. "The reality is that most people in this country are overweight and they need to get into an exercise program," he said.

"I think fat people should lighten up," said Jerry Della Femina, a New York advertising executive who describes himself as "fat." "There is nothing wrong with that billboard, but I like the fact that people are now marching. It is good exercise. There's nothing to the poster. It's funny," he said.

> "Despite the protests from fat activists, the health club said it has no plans to change its advertisements."

capsule

Ectopic pregnancies can be more common after in vitro fertilization Women who have tubal problems have an increased risk of ectopic pregnancies. Unfortunately that risk persists if they have in vitro fertilization (*Fertility and Sterility* 1999; 71:282-6) according to a study of over 700 women. The study found that myomectomy may also be a risk factor for ectopic pregnancy.

Speaker's Corner

A memorable incident: when a shovel should be an agricultural implement

see also p.297

I was a visiting professor of anesthesiology in a hospital outside the United Kingdom when I was asked to see an emergency admission with a severe hematemesis. The patient was elderly, wasted, disoriented, somewhat dehydrated, hypotensive, and tachycardic. He had a chronic gastric ulcer. He had been an inmate of the local mental hospital for the previous 20 years. He was a Jehovah's Witness. His medical superintendent had left the decision about blood transfusion to his wife, who was on her way in. The surgeon would accept my decision about whether to operate.

I was incensed. Such hypocrisy, such cant, a shovel was a shovel and not an agricultural implement. "You mean if he dies," I snapped.

I saw the wife wince and her hand stretch out towards the pastor, who held it gently. Then she said slowly, "He was a good man doctor, before he became ill. You will do your best, please, won't you. But no blood. To him, it would not be right." After that I had no choice.

The surgeon agreed to do the minimum, just undersew the bleeding ulcer and stop the bleeding. I would keep the patient alive.

"Doctor, you do not understand. We mean, if he should go to sleep, that is cross over, pass away."

I telephoned the chief administrator. He would not give permission but would consult the minister of health (it was that sort of country) as the state was legally responsible for the patient's welfare. Within 10 minutes (it really was that sort of country), the reply came. The doctors should sort it out with the patient's wife.

We met the wife in the boardroom. An elderly, shy woman, she was accompanied by a younger Pickwickian man, her pastor. Harshly I explained that without the operation the husband would die; with the operation but without blood there was just an outside chance of survival. If blood was available there was a very good chance that he would survive. The reply stunned me.

"If he should go to sleep," said the pastor. I interrupted, "Of course he will go to sleep. That is why I am here." Again the statement, "If he should go to sleep, if God wills that he goes to sleep."

I interrupted rather angrily: "Yes, he will go to sleep. I will make sure of that, that is up to me, not God." Another interruption: "Doctor, you do not understand. We mean, if he should go to sleep, that is cross over, pass away."

The surgeon kept to his word. The ulcer was easily located and swiftly undersewn. I juggled with plasma expanders and salt solutions to correct the patient's blood volume and dehydration, to keep him pain free and relaxed. But his blood pressure stayed ominously low.

The peritoneum was closed, and I breathed a sigh of relief mixed with pride at my achievement. Then came a soft cry from the surgeon. A subcutaneous stitch had hit a vein somewhere. By the time it was located, 30 ml of blood were lost. The patient's blood pressure fell irrecoverably and he died.

What did I learn? Humility was one lesson. I might know it all, but I was not God. Bullying people to accept my beliefs was wrong, especially when they obviously knew they were further endangering the life of someone they loved dearly. Their own moral dilemma was a hard enough burden. The remaining lesson? Euphemisms do have a place in providing comfort to the distressed. But 25 years later I still wonder if I was right clinically.

PJ Tomlin, MD
Retired Anesthetist,
Rodnar House, The Headland
Downton, Wiltshire SP5 3HJ, UK

Letter from the Northwest

From academia to private medicine: where did the profession go?

John Roberts, From the Madrona Medical Group, Northwest Campus, Bellingham, WA 98225; jcroberts@hinet.org

"I didn't come here to take care of patients, and I'll leave if I have to," said one doctor after another. We members of the Department of Medicine at Johns Hopkins University had been summoned by the chairman. Academic centers were being viewed suspiciously by managed care organizations. We were seen as pits of wasteful care and bastions of unnecessary tenure. The chairman announced that patient care must be returned primarily to senior doctors, and trainees should once again become trainees.

The faculty's response, nearly unanimous, was the signal that academia was not where I belonged. Like most physicians I entered medicine to help the infirm. By the time I finished training, I felt I owed those coming behind me. So I took up teaching.

But teaching is not the foundation of medical schools. Research is. Teaching is seen by many researchers as incarceration on teaching wards for a couple of months each year. And if teaching is incarceration, then direct patient contact is akin to isolation. Even William Osler, medicine's deity, is said to have fled to England when he was forced to see more than half a dozen patients a day.

Is it any wonder that fewer than half of medical school faculty members are role models for doctors in training?[1] The doctors who abhor patient care and only reluctantly share their clinical wisdom with residents are poor models. Further, as a young teacher, I found myself wanting for wisdom to provide; I had never practiced medicine outside the walls of academia. I was once a journalist. In those days, journalism schools rarely hired a faculty member who had fewer than 10 years of actual journalism experience. (Sad to say, that practice has also given way to a professional academician, the journalism professor who has never worked as a journalist.)

As a member of the medical academic elite, I had time to read the four major weekly journals and more, attend at least two hour-long committee meetings each week, and see patients during my regular clinical hours—four days a week.

So I left. I went from the tower to the trenches, to private practice. Today, I see 80 patients a week, rather than eight. I only occasionally spend my time on hospital services because my patients generally live outside a hospital. When the call comes at 3AM, no resident answers the phone—I do. My teaching is provided solely to patients, not to students or residents.

Today I practice skills never taught in my training. The internal medicine I learned is a minority of my practice. Depression, dermatology, orthopedics, angry patients, addicted patients, somatizing patients and business skills—only a few are part of the traditional medical curriculum.

Today I rarely attend committee meetings. Each hour at the table is an hour that deprives patients of their doctor, and me of an income.

Today, I struggle to read even one journal a week, usually as I fall off to sleep. I understand why *Medical Economics* is the most read "journal" among US doctors. My academic interests were on getting research into practice. This seems irrelevant nowadays. It is not clinical research that drives much of my behavior, but the contractual arrangements that put me at financial risk with each patient encounter. A British academic general practitioner once said to me, "The only thing that will change a doctor's practice is money." I cannot argue.

The ethics of academics disquieted me—spending research grant money on committee meetings, forcing residents to do absurd hours for a pittance. But my ethics in private practice also seem inglorious—so much is driven by dollars. For example, if diabetes education does not pay my group practice, then it won't get done, even if it is the right thing to do for newly diagnosed diabetics. If a referral to a consultant is going to cost me money, I hesitate to offer it. In our group we judge our performance by money saved. I have seen no evidence that such measures are markers for clinical quality.

The studies in the *New England Journal of Medicine* earlier this year that show teaching hospitals have better outcomes for some common conditions should come as no surprise.[2, 3] The accompanying editorial said that more eyes on a patient made for more careful decision making.[4] What isn't talked about is money. In private medicine, if I cannot make money, I am less likely to pursue that clinical course. On the positive side I know our patients more intimately, so I hope this mitigates my greed.

We doctors claim to be a profession. But in neither academic nor private medicine, do I see the evidence. The disregard of teaching and of patient care in institutions said to be devoted to these ideals is the lie of academics. The overpowering greed for money in private medicine shames me too much to call myself a professional.

Still, both academic and private medicine are filled with enough wonderful aspects that, if shared between them, would place physicians back in the noble place we feel we belong. Private medicine needs the constant questioning of every decision—the hallmark of the teaching institution. Academic medicine needs to learn the skills of everyday practice to teach young doctors. And academics could learn from the rich relationships that keep private physicians coming to work each day.

Sadly, such sharing is unlikely to happen soon. The barriers, both political and personal, are too great. We might all do well to ask ourselves if we are too comfortable to make the sacrifices needed to transform medicine back into a noble profession.

References

1. Wright SM, Kern DE, Kolodner K, Howard DM, Brancati FL. Attributes of excellent attending-physician role models. *N Engl J Med* 1998; 339:1986-93.
2. Chen J, Radofrod MJ, Wang Y, Marciniak TA, Krumholz HM. Do "America's best hospitals" perform better for acute myocardial infarction? *N Eng J Med* 1999; 340:286-92.
3. Taylor DH, Whellan DJ, Sloan FA. Effects of admissions to a teaching hospital on the cost and quality of care for Medicare beneficiaries. *N Eng J Med* 1999; 340:293-9.
4. Kassirer JP. Hospitals, heal yourselves. *N Eng J Med* 1999; 304:309-10.

Panning for gold. *Courtesy of Wells Fargo Historical Services, San Francisco, CA 94163*

BOOK REVIEW

The New Encyclopedia of the American West

by Howard R. Lamar, Yale University Press, 1998, $60.00

A case cannot be made for this handsome volume enhancing physicians' skills or understanding. It has no entry for medicine, despite western medical service, policy, or research, and it ignores the Oregon Health Plan—the first example of a peacetime government explicitly rationing health care. There is meager mention of the one fatality in Lewis and Clark's expedition—a member who died a few weeks out at Council Bluffs, Iowa, probably from a ruptured appendix. The book neglects mentioning that Lewis and Clark used medical services to help negotiate peaceful passage across the many domains of Native Americans. The squaws brought their children along for medical treatment, and the warriors were happy to let the benefactors pass without harm. There is no detail of the time Clark spent with Dr Benjamin Rush in Philadelphia, learning about medicine. Rush gave Clark powerful emetics to carry along, and the men would joke about "Rush's bullets." So why would any physician wish to buy this historical encyclopedia, as I did, prior to being asked to review it? My interest chiefly lay in learning about the "winning of the West," that latter day crusade pursued with the zeal of the 11th century quest of Jerusalem.

Most readers will buy the 1,324 pages of alphabetically ordered passages to further their childhood imagination. The magic of the Wild West is made real in the universal childhood game of cowboys and Indians, a necessary part of growing up to become a red-blooded American.

Perhaps it is asking too much of an encyclopedia to convey, among the parade of facts, the passion involved in the winning of the West. Some passion is there, but scattered among the references. Fenimore Cooper's Natty Bumppo of the early forest gives way to Mike Fink of the Mississippi, then to Deadwood Dick and Calamity Jane of dime novels fame. Then comes Wild Bill Cody with his Indian sidekicks' traveling road show, who evolves into Tom Mix and Hoot Gibson and then into John Wayne, the Zeus of Hollywood.

Perhaps too, it needs more than a brief reference in the "Environmental History of the West," for insight into the present western environmental guerrilla war. The clear-cut wilderness between the Pacific Ocean and Northwest Cascade, euphemistically called "shelter wood cut" by the Forest Service, is referred to in the encyclopedia as forest. This is far from factual when only five percent of the original forest remains intact.

There's a similar problem with the "Fisheries" section, in which little mention is made of the plight of exploited salmon. The encyclopedia states, "Because all sides rejected the idea of limited participation, a central feature of fishing regulation in the West has been inefficiency." Nothing is mentioned of the fish fights of the 1880s when gill netters and trap fishermen ambushed each other while also fighting the canneries—forcing the governor to call out the National Guard.

Under "Reclamation and Irrigation," mention is made of the Bureau of Reclamation becoming the target of the "new conservationists," but the fierce battles going on between industry and agriculture and concerned citizens over deconstructing the West's mighty dams are not detailed.

The change in America's attitude from believing in unlimited resources to realizing people must work together to preserve the environment appears as scholarly notes rather than the next stage in the crusade to save the West. It's like reading an encyclopedia of Western Europe that fails to mention World War II.

The references reveal more omissions than errors. C.S. Price, the recognized Western artist, is referenced, yet John Reed, his contemporary Portlander, a world recognized journalist, draws a blank. The material on the lost state of Franklin is excellent but where is the proposed state of Jefferson, that unborn political ambition of the northern tier of California and the southern tier of Oregon counties, which for so long has tempted them to break away and form an "authentic" Western state?

If you are uninterested in a message but happy in a series of good reads, settle down to this book. The full and accurate account of the fur trade, with its rapscallion murderers out to kill each other, most Native Americans, and all the beavers in the West is, alone, worth the price. Lamar's account of the vast pageant of questing voyagers—men, women and children—must hold your interest, while haunting readers with the unspoken question of why people remain intent on destroying so much of what we have been blessed with.

Ralph Crawshaw
Clinical Professor of Psychiatry,
Clinical Professor of Public and Environmental Health,
Oregon Health Services University,
Portland, OR 97210;
RCKOS@imagina.com

Poetry

POETS AND HEALERS

Janice Willms
3843 Center Avenue,
Santa Barbara CA 93110

When they ask me, as of late they frequently do, how I have for so many years continued an equal interest in medicine and the poem, I reply that they amount for me to nearly the same thing.

William Carlos Williams from *Autobiography*

When contemplating the value of the poem to the healer, one only has to recall the number of physicians who take up the pen. Why does this happen? What is it about putting in words the joy and the sorrow, the sense of power juxtaposed against feelings of helplessness, the failures and successes that make up the profession's daily menu? If you are a poet, closeted or published, you know the answer.

Not only doctors and nurses write poems about their work and their patients, but patients write poems about their illnesses and their caregivers. The patient's muse may be a different one than he or she who guides the physician-poet, but the healing force is similar.

A case could be made for every member of our profession giving consideration to the voices of both colleagues and patients to more clearly appreciate what we are about. One need not write poetry to be able to read it, and to thereby learn more about the human condition. "Poetry!" you retort. "Whatever has poetry to do with me? To begin with, I find it unaccessible, I do not understand it, it seems trivial." In a poem called *Poetry,* Marianne Moore recognizes and addresses these concerns, "I, too, dislike it: there are things that are important beyond all this fiddle./ Reading it, however, with a perfect contempt for it, one discovers in/ it, after all, a place for the genuine." And the "genuine," the rawness of human experience, may become the window through which we can understand ourselves and our fellows.

FIRE SHADOWS

Gwen Head
72 Eucalyptus Road, Berkeley, CA 94705

Disorder and Early Sorrow

Help me, Dr. Joyce Brothers.
What would *you* do
with one kid, twenty, male, outdoors lamenting,
worst among many woes, his dilatory
and probably irremediable virginity?

And indoors, another, female, fifteen, dead
still for two hours behind a locked bathroom door—
not a whimper, retch, or flush?

Outdoors, the vagabond son of an old friend,
is not really outdoors. His habitat is a hermitage
on wheels, a much-recycled
Volkswagen camper craggy with spare batteries,
fuses, Pennzoil, Pop Tarts,
its ornamental foliage four weeks' worth
of unwashed laundry.
His *wanderjahr* is gilt-edged, his depression
soothed by a single plastic, multi-purpose
tool. Issued by AmEx to his trust,
it's less confusing than a forty-two
piece wrench set,
or a woman.

Indoors, again entreated, soundlessly
slides dead-bolt back, and manifests herself
hunched, mussy, tear-slimed, shuddering
between the bathtub's claws.
She's downed
the shower-curtain rod, spewed hoarded ribbons,
earrings, barrettes, eyeliner, hosed the whole
mess down with shampoo and peroxide—
even the fallen shower curtain, knotted
with pantyhose, even the tattered
copies of *Vogue.*

What *I* could do, Dr. Joyce, wasn't much. Outdoors,
ravenous with grief, requested a ham
sandwich. No, make that two,
with lettuce, tomato, mayo.
Indoors preferred to order off the menu:
one soap opera, madhouse, gun.

Ballade: Self and Not-Self

These things start early. Each time you came in
to your own room after absence, you would seek
out favorite books, toys, animals; first check
each idiosyncrasy of fur, wheel, spine,
then gather and marshall them all. A stout front line
might not hold fast. No, each must be one spoke
in a stilled circumference that would not break,
whatever the steep velocity of time.
These are my things, the things that make me mine.

Christmas, fifteen years later. Welcomed back,
you practiced aversion, shut doors and lowered blinds.
Regurgitated grass, fur, bone bits, rug twine—
the hall was your hairball. Bilious, you brooked
no taste of others, but upchucked my alarm clock,
your father's sock, an old friend's Valentine,
like a prissy old cat—you whom I thought my kitten!—
to feast on dead dolls, eyes blank, limbs stained, manes hacked.
These are my things, the things that make me mine.

Where you've sent yourself now, the staff had never seen
or toted so much identity. Swiftly locked
down, you relaxed.
Next day I scrabbled through seawrack
in your fetid basement: spavined slingbacks, magazines,
dirty clothes, journals, music-boxes, knick nacks,
mirrors, earrings, sewing kits unraveling…
And shopping-bagged stashes of Lithium, Depakote, Navane.
And your baby powder spilled, dispersed like smoke.

These were my things, the things that made me mine.

POETS AND HEALERS cont'd

Poetry—the creation or the reading of poetry—is one form of healing. Robert Coles gave early impetus to the idea of stories as a means of better understanding one's patients in his treatise *The Call of Stories.*[1] Using works of fiction and poetry, Coles shows we can learn about others through the power of storytelling—not just the history of the present illness as we traditionally structure it—but the life story that underlies the meaning of illness to the patient. Howard Brody expands upon this when he discusses the importance of the life story to the sufferer's perception of his or her change in position brought on by an illness that alters expectations.[2] The "stories" referred to by Coles and Brady may be in the form of oral histories, prose accounts, and poetic expressions of fears and hopes. Not only do these life stories help patients formulate their own positions, but they are of great help to professionals who are trying to deal with the wide variation in patient responses to pain, unhappy diagnoses, frightening treatments, and uncertain outcomes.

Examples of patient perceptions, often not expressed in ordinary patient-doctor dialogue but appearing in the poetic images conjured by the sufferer, may solve a multitude of mysteries. A review of poems, for example, of women having treatment for breast cancer, provides insight into such "problems" as resistance to certain forms of therapy, and fears the doctor may never have considered, and may lead to helpful changes in management strategies.

We pride ourselves in our listening skills. But listening must go beyond the facts of the symptoms and pass into learning what these details mean to the patient. This heightened awareness can be helped by reading the poetry of those who have become "victims" of illness.

But patients are not the only ones who heal by means of poetry. Ours is a "sickening" profession at times. If we are at all in touch with our humanity, we must feel our own sickness of heart and soul as we deal with the suffering of others. Williams sees no difference between medicine and poetry.

POETS AND HEALERS cont'd

In his eyes they are variations on the same theme: to be human is to suffer, and suffering requires description. Unlike most of us, Williams and his poetically gifted colleagues are able to write well enough to both heal the writer and provide assurance to the reader. We do not all have the gift of poetry, but we can all read. And by engaging ourselves with these expressions of our common agonies and joys, we can affirm our humanity.

The poems of our colleagues can reassure us that we are not alone. There is no doubt, sense of guilt, or inadequacy that others of us have not felt. As a group, we don't comfortably share these feelings, which expose our Achilles' tendons, our failings. Even if we cannot speak aloud to one another, we can commune through poetry. For example, how easy is it to admit that we don't always like our patients? Dannie Abse takes this burden on his own shoulders in his short poem, *The Doctor.* He admits his guilt and allows us to share it.[3] In addition to his poems about the pain of failure, John Stone writes of the power, the glory, and the sacred covenant assumed upon becoming a physician in *Gaudeamus Igitur.*[4] With him we can celebrate the privilege of being doctors. Others have written of the meaning to them of losing a favored patient or a family member for whom they have cared, or the ambivalence of "pulling the plug." We have all been there. Isn't it comforting to know that others have been also, and only differ from us in their ability to create the words to express what we feel.

If you haven't yet, healer, try poetry. To discover its gifts and its value to us as professionals is a wonderment worth experiencing.

1. Coles R. *The Call of Stories.* Boston: Houghton Mifflin, 1989.
2. Brody H. *Stories of Sickness.* New Haven: Yale UP, 1987.
3. Abse, D. *Poems from the Medical World.* Lancaster: MTP Press Ltd., 1980; 16.
4. Stone J. *Renaming the Streets.* Baton Rouge: Louisiana State UP, 1985; 21.

These poems are from Gwen Head's fourth collection of poetry, *Fire Shadows*, which will be published by the Louisiana State University Press. Her other books are *Special Effects*, *The Ten Thousandth Night*, and *Frequencies: A Gamut of Poems*. Head's poems, fiction, and essays have appeared in *The American Poetry Review*, *The Yale Review*, *American Voice*, *The Southern Review*, and *Ballet Review*, among many other publications. She has taught at the Iowa Writers Workshop and the University of California, Davis, as well as many writers conferences. Of these, her favorite is the Writers at Work Conference in Park City, Utah, where she met her husband, biographer Bernard Taper. Head's honors include a 1995 Literature Fellowship from the National Endowment for the Arts that supported the completion of *Fire Shadows*.

Classified Advertisements

The rate for each insertion is $1.50 per word, with a minimum of 30 words ($45). A word is defined as one or more letters bounded by spaces. Bold type face is available at no extra charge. Confidential box numbers are available for an extra $10 per insertion. Classified advertisement are payable in advance by check, AMEX, VISA or MasterCard.

To place your ad, contact:
Ruth Staunton,
WJM Western Journal of Medicine,
221 Main Street, PO Box 7690,
San Francisco, CA 94120-7690,
Tel 415-974-1071, Fax 415-882-3379
rstaunton@bmjgroup.com

Classified Display Advertising

The classified display rate is $70 per vertical inch. Maximum sizes: 1 column by 5 inches or 2 columns by 2 inches ($2\frac{1}{8}$ inches per column). Larger classified ad space available on request. Please supply camera-ready artwork if logos or other art are included in the ad. Copy for classified advertisements should be received no later than the first of the month preceding issue. All copy must be typed or printed, we prefer to receive copy electronically as e-mail or on a disk.

MEETINGS/CONFERENCES

The ACC/SCA&I Board Review Program: Interventional Cardiology, October 14-17, 1999, the Westin Peachtree Plaza, Atlanta, Georgia. Sponsored by the American College of Cardiology, and the Society for Cardiac Angiography and Interventions. Program Directors: George W Vetrovec, MD, FACC, FSCAI, and Morton J Kern, MD, FACC, FSCAI; 21 category 1 credit hours. **Information:** 800-253-4636, ext. 695, fax 301-897-9745.

WESTERN STATES OPENINGS

Many multispecialty groups and hospitals have asked us to recruit for over 100 positions of various specialties. Both permanent and locum tenens. Send CV to:

Western States Physician Services
7510 No. Trellis Circle, Fresno, CA 93720
Call 800-873-0786, fax 800-705-7943
e-mail weserve@lightspeed.net

★ ★ ★ ★ ★ ★

ENJOY A SEASIDE VACATION IN SAN DIEGO!

San Diego Academy of Family Physicians' 43rd Annual Postgraduate Symposium "Family Medicine Update: 1999" Hotel Del Coronado • Coronado, California July 9-11, 1999

This SDAFP Symposium features a variety of educational lectures and specialty workshops. This program has been accredited by the AAFP for 19 Category 1 CME credit hours. The SDAFP is an approved provider for this program by the AOA, AAPA, and Boards' of Pharmacy and Registered Nursing.

Many entertaining social activities have been planned for the whole family, so don't miss this opportunity to combine top quality continuing medical education with a fun family vacation.

To receive a detailed brochure, call, fax or write to:

SAN DIEGO ACADEMY OF FAMILY PHYSICIANS
P.O. Box 5996, Chula Vista, California 91912
(619) 422-1186 FAX (619) 476-1536

PHYSICIANS WANTED

California Coastal Community: Mid-size multi-specialty group has opening for BC-BE Internal Medicine and Family Practitioners. Ventura is located 65 miles north of Los Angeles, has excellent schools, sunny beaches, friendly atmosphere, and a wide range of cultural/recreational activities. Attractive compensation and benefit package. **Contact:** Physician Recruitment; Buenaventura Medical Group, 2705 Loma Vista Rd., Ventura, CA 93003; 805-652-5240 or fax CV to 805-652 5299.

California, Northern: Internist needed for 70+ physician group affiliated with Catholic Healthcare West. Hospital and office based practice (50/50) with shared call, competitive income and comprehensive benefits. **Contact:** Danise Cooper; 800-765-3055, ID#: 6400WE, fax 314-726-3009, e-mail dcooper@cejka.com. Visit our website at www.cejka.com.

Salem/Willamette Valley–Salem Clinic, PC: a 40-physician multi-specialty group located in Salem, Oregon, is currently recruiting a full-time Internal Medicine physician. The position consists of a $4\frac{1}{2}$-day workweek. Salem Clinic offers a comprehensive benefit package and competitive income guarantee with opportunity for rapid incorporation into production formula. 1:7 call, single hospital town. If interested, please forward, fax or e-mail a copy of your CV. **Contact:** Sherry Krog, Salem Clinic, PC, 2020 Capitol St. NE, Salem, OR; 503-399-2470, fax 503-375-7429, e-mail gunderBL@aol.com.

California–Monterey Bay: Full/Part-time positions. 12 clinic urgent care system seeking BC/BE, EM/FP physicians. Work 2-3 days/week with 4-5 days off! Benefits include competitive compensation, malpractice insurance paid, 401k & health insurance. Practice in California's most beautiful coastal recreational area. **Contact:** Donaldo M Hernandez, MD at 831-622-8400; Send CV to Medical Director, Doctors on Duty, 100 Clock Tower Pl., #220, Carmel, CA 93923; fax 831-622-8401, or e-mail mmcmilla@doctorsonduty.com.

IM/FP, BC/BE, Post Falls, ID: Rapidly growing Primary Care practice. Possible part-time. Hospital privileges required. Salary 3-6 mos, then production. Need WA&ID licenses. **Contact:** Michael Carraher MD, 208-773-0721.

Northern California Wine Country: Mendocino Community Health Clinic seeks caring, motivated individual for work in clinic and hospital, including ICU. NO OB. Pure air, gorgeous country, 40 minutes to coast, 2 hours to SF. No managed care. Superb compensation. No J1 positions available. **Contact:** Carole Watkins, Director of Human Resources; fax resume, 707-468-0174.

Continuing Medical Education

ARIZONA ● CALIFORNIA, HAWAII, NEVADA ● COLORADO ● IDAHO ● NEW MEXICO ● UTAH ● WASHINGTON ● WYOMING

ARIZONA

All courses listed have been certified as meeting the criteria for Category I of the ArMA CME Certificate and the AMA Physicians Recognition Award. To list Category I CME programs, please send information to Arizona Medical Association, 810 West Bethany Home Road, Phoenix, AZ 85013; or phone 602-246-8901.

Brochures and registration forms are available from the contact person or organization sponsoring the program.

OCTOBER 29-31, 1999: Neurology for the Non-Neurologist. The Phoenician, Scottsdale, AZ. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; tel 800-421-3756; fax 303-798-5731.

DECEMBER 10-12, 1999: Managing Respiratory Disease. The Phoenician, Scottsdale, AZ. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; tel 800-421-3756; fax 303-798-5731.

CONTACT INFORMATION

Mayo Clinic-Scottsdale Contact—Postgraduate Courses, Mayo Clinic-Scottsdale, 602-301-7447; **U of A Contact**—University of Arizona College of Medicine, Arizona Health Sciences Center, Tucson, AZ 85724. 520-626-7832; 800-328-5868.

CALIFORNIA, HAWAII, NEVADA

All courses and meetings listed are approved for Category I credit toward the CMA Certificate in CME. To list accredited courses here, please send information at least two months in advance to Paulette Richardson, Continuing Medical Education, California Medical Association, PO Box 7690, San Francisco 94120-7690; or phone 415-882-3387. For more information on accreditation or certification, please write to the above address.

ALLERGY/IMMUNIZATION

AUGUST 13-15, 1999: A Midsummer Night's Wheeze. California Society of Allergy, Asthma and Immunology at La Costa Resort and Spa, Carlsbad, CA. 12 hrs. $145-$199. Contact: CSAAI Conference Management; tel 714-828-8022.

ANESTHESIOLOGY

NOVEMBER 5-7, 1999: 11th Annual Anesthesiology Update. Monterey Plaza, Monterey, California. Contact: 916-734-5390.

EMERGENCY MEDICINE

JUNE 3-4, 1999: Improving Emergency Department Patient Satisfaction and Reducing Length of Stay. Holiday Inn Chicago City Centre, Chicago, IL. Contact: CEME, 5330 Primrose Drive, Suite 250, Fair Oaks, CA 95628; tel 800-651-2363.

AUGUST 16-19, 1999: National Emergency Medicine Board Review. American College of Emergency Physicians at Harrah's Las Vegas, NV. Mon-Thurs. 40 hrs. $895. Contact: Center for Emergency Medical Education 800-651-CEME (2363).

ENDOCRINOLOGY

OCTOBER 22-24, 1999: Clinical Endocrinology for Primary Care Physicians. Tropicana, Las Vegas, NV. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; tel 800-421-3756; fax 303-798-5731.

ETHICS

SEPTEMBER 22-25, 1999: Legal Issues in Damaged Brain Injury Cases. UC Davis at Westin St. Francis Hotel, San Francisco, CA. Contact: UCD 916-734-5390.

FAMILY PRACTICE/PRIMARY CARE

JUNE 5-7, 1999: 8th Annual Primary Care Treatment of Pain. UC Davis at Tenaya Lodge at Yosemite Fish Camp, CA. Contact: UCD 916-734-5390

JUNE 13-18, 1999: 23rd Annual Fingers to the Toes Primary Care Orthopædics. UC Davis at Stanford Sierra Camp, near South Lake Tahoe. Contact: UCD 916-734-5390

JUNE 25-27, 1999: Dermatology for the Non-Dermatologist. Medical Education Resources at the Hyatt Regency Alicante, Anaheim, CA. 11 hrs. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Ct., Ste. 500, Littleton, CO 80120-4569; tel 800-421-3756.

JULY 5-8, 1999: Family Practice Board Review Course. UCSF at Fairmont Hotel, San Francisco, CA. 25 hrs $525-$575. Contact: Program Coordinator, Dept. Family and Community Medicine, 500 Parnassus Ave, MU-3E, SF, CA 94143-0900; tel 415-476-5250.

JULY 25-29, 1999: 19th Annual Current Concepts in Primary Care Cardiology. UC Davis at Granlibakken Conference Center, Tahoe City, CA. Contact: UCD 916-734-5390.

JULY 30-AUGUST 1, 1999: Coronary Heart Disease Update. Medical Education Resources at Tenaya Lodge, Yosemite, CA. 11 hrs. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Ct., Ste. 500, Littleton, CO 80120-4569; tel 800-421-3756.

AUGUST 6-8, 1999: Managing Respiratory Diseases. Medical Education Resources at the Hyatt Regency Monterey, CA. 11 hrs. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Ct., Ste. 500, Littleton, CO 80120-4569; tel 800-421-3756.

INTERNAL MEDICINE

AUGUST 22-27, 1999: New Advances in Internal Medicine. UC Davis at Embassy Suites, Monterey, CA. Contact: UCD 916-734-5390.

OB/GYN

SEPTEMBER 25-26, 1999: Ultrasound Update: 1999. Hilton Hotel, Sacramento, CA. 916-734-5390.

DECEMBER 10-12, 1999: Issues in Women's Health. Tropicana, Las Vegas, NV. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; tel 800-421-3756; fax 303-798-5731.

OCCUPATIONAL & ENVIRONMENTAL

AUGUST 5-6, 1999: Occupational & Environmental Toxicology for the Health & Safety Professional. UC Berkeley. Holiday Inn Bay Bridge, Emeryville, CA. Contact: Center for Occupational & Environmental Health, UC Berkeley, Richmond Field Station, 1301 S. 46th St., Bldg. 102, Richmond, CA 94804; tel 510-231-5645; http://socrates.berkeley.edu/~coehce/.

ORTHOPEDICS

JUNE 13-18, 1999: 23rd Annual Fingers to the Toes Primary Care Orthopædics. Stanford Sierra Camp, near South Lake Tahoe, Fallen Leaf Lake, CA. Contact: 916-734-5390.

PEDIATRICS

JUNE 4-7, 1999: Pediatric Environmental Health: Putting It Into Practice. Children's Environmental Health Network. Westin St. Francis, San Francisco, CA. $250-350. Contact: Children's Environmental Health Network, 510-597-1393, ext. 14, or cehn@cehn.org.

JULY 16-17, 1999: Seventh Annual Pediatric Update. Sponsored by Lucile Packard Children's Health Services at Stanford and faculty from UCSF and Stanford Schools of Medicine. Lucile Packard Children's Hospital. Contact: Elinor Meyer, Continuing Medical Education and Physician Relations Department, Lucile Packard Children's Hospital, 725 Welch Road, Palo Alto, CA 94304; tel 650-497-8554.

PRIMARY CARE

JUNE 5-7, 1999: 8th Annual Primary Care Treatment of Pain. Tenaya Lodge at Yosemite, Fish Camp, CA; tel 916-734-5390.

JULY 25-29, 1999: 19th Annual Current Concepts in Primary Care Cardiology. Granlibakken Conference Center, Tahoe City, CA; 916-734-5390.

OCTOBER 22-24, 1999: Clinical Endocrinology for Primary Care Physicians. Tropicana, Las Vegas, NV. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; tel 800-421-3756; fax 303-798-5731.

RADIOLOGY

SEPTEMBER 25-26, 1999: Ultrasound Update: 1999. UC Davis at Hilton Hotel, Sacramento, CA. Contact: UCD 916-734-5390.

GENERAL/MULTIDISCIPLINARY

JUNE 22-29, 1999: Wellness in Practice: Mindfulness-Based Stress Reduction in Mind/Body Medicine. Enloe Medical Center at Mana Lea Retreat Center, Maui. Contact: Maui Stress Reduction Retreats, Steve; tel 530-898-1495.

AUGUST 24-25, 1999: BLS Instructor Course. American Heart Association at San Leandro. 11 hrs. Contact: CPR Seminars; tel 925-754-7900.

OCTOBER 15-17, 1999: Physician Leadership Program. California Academy of Family Physicians at Laurel Heights Conference Center, SF. 20 hrs. $1,245-$1,395. Contact: Laura Johnson Morasch; tel 415-394-9121; www.familydocs.org/ Orgs?hcli.html; e-mail: HCLI@familydocs.org.

LOSS PREVENTION

SEPTEMBER 22-25, 1999: Legal Issues in Damaged Brain Injury Cases. Westin St. Francis Hotel, San Francisco, CA; Contact: 916-734-5390.

HOME STUDY/SELF ASSESSMENT

California Physicians' Legal Handbook Series. California Medical Association. Contact: CMA, PO Box 7690, San Francisco 94120-7690; tel 800-882-1262.

Breast Cancer, Early Detection and Control. Texas Medical Association. CD rom. $70. 2 hrs. Contact: Texas Medical Association; tel 800-880-1300; http://www.texmed.org/health_science/hs_poep.html

COLORADO

To list CME programs here, please send information at least two months in advance to: Mr Robert L. Kennedy, Denver Medical Society, 1850 Williams Street, Denver, CO 80218; or phone 303-377-1850. Brochures, course information, and registration forms are available from the contact person or organization.

TUESDAY NOON CONFERENCES: Various Topics in Medicine. Lutheran Medical Center, Wheat Ridge. Contact: Jean A. Kline; tel 303-425-2951.

FIRST WEDNESDAY OF EACH MONTH: Various Topics in Neurology. Colorado Society of Clinical Neurologists. Contact: Colorado Society of Neurologists; tel 303-449-3566.

SECOND WEDNESDAY OF EACH MONTH: Cardiovascular Education Series. St Anthony Hospital at St Anthony Hospital, Denver. Contact: Rose Powell; tel 303-629-3678.

JUNE 17-19, 1999: Issues in Women's Health. Hyatt Regency, Grand Cayman. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; tel 800-421-3756, 303-798-9682 or fax 303-798-5731.

JUNE 18-20, 1999: Neurology For The Non-Neurologist. Buena Vista Palace, Orlando, FL. Fee $375. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; tel 800-421-3756, 303-798-9682 or fax 303-798-5731.

JUNE 24-26, 1999: Clinical Endocrinology For Primary Care Physicans. Sonesta Beach Resort, Bermuda. Fee $375. Contact: Linda Main, Meetings Coordinator; MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; tel 800-421-3756 or 303-798-9682; fax 303-798-5731.

JUNE 25-27, 1999: Coronary Heart Disease Update. Sheraton Fiesta Beach Resort, S. Padre Island, TX. Fee $375. Contact: Linda Main, Meetings Coordinator; MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; tel 800-421-3756 or 303-798-9682; fax 303-798-5731.

CONTACT INFORMATION
U of Colo—Contact: University of Colorado Health Sciences Center, School of Medicine, Office of Continuing Medical Education, 4200 E 9th Ave, Denver 80262; phone 303-372-9050 or 800-882-9153; fax 303-372-9065.

IDAHO

To list CME programs here, please send information at least two months in advance to:
Ada County Medical Society, Inc. 305 W. Jefferson, PO Box 2668, Boise, Idaho 83701; phone 208-336-2930. Brochures, course information, and registration forms are available from the contact person or organization.

NEW MEXICO

Information, requests for accreditation, and items to be listed should be sent to the chair of the CME Committee, New Mexico Medical Society, 7770 Jefferson, Suite 400, Albuquerque, NM 87109, at least two months in advance. For information on CME accreditation or on the CME requirements of the New Mexico Board of Medical Examiners, please write to the above address or phone 505-828-0237.

NOTE: Course information in the following listing is subject to change on occasion. Check with the sponsoring institution for current details.

EVERY FIRST AND THIRD TUESDAY: Building and Implementing Clinical Practice Guidelines at the Point of Care. Contact: Thomas A. Naegele, DO; tel 505-275-7267.

JULY 30-AUGUST 1, 1999: Neurology for the Non-Neurologist. Eldorado Hotel, Sante Fe, NM. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator; MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; tel 800-421-3756; fax 303-798-5731.

SATELLITE COURSES
CONTACT: Joe Treat or Jim Cato, Immunization Program; tel 505-827-2366.

CONTACT INFORMATION
UNMSOM—University of New Mexico School of Medicine, Office of CME, PO Box 713, Albuquerque NM 87131; tel 505-277-3942.

UTAH

All courses listed meet the criteria for Category 1 of the Physician's Recognition Award of the AMA. To list AMA Category 1 CME courses, send information at least two months in advance to the Office of Continuing Medical Education, 540 East Fifth South, Salt Lake City, UT 84102; or phone 801-355-7477. For information on CME accreditation, please write the CME office at the above address. NOTE: Course information in the following listing is subject to change on occasion. Check with the sponsoring institution.

MEDICAL GRAND ROUNDS

Weekly: Grand Rounds in Internal Medicine, Psychiatry, OB/GYN, and Pediatrics. Contact: UUSM.

Weekly: Pediatric Grand Rounds. Contact: PCMC.

WASHINGTON

The listing of continuing medical education programs in Washington state is compiled by the Washington State Medical Association. To list Category 1 programs here, please send information at least two months in advance to Continuing Medical Education, Washington State Medical Association, 2033 Sixth Avenue, Suite 1100, Seattle, WA98121; or phone 206-441-9762 or 800-552-0612.

Brochures and registration forms are available from the contact person or organization listed at the end of each course or in the list of course sponsors and contact information.

COURSE SPONSORS AND CONTACT INFORMATION

CME HARBORVIEW—Contact: Gayle Splater, Cytology Continuing Education, Dept. of Pathology, Harborview Medical Center, 325 Ninth Ave, Seattle, WA 98104; tel 206-223-5953.
PCMS CME—Contact: Executive Director, College of Medical Education, 705 S Ninth, No. 203, Tacoma, WA 98405; tel 206-627-7137.
U/W (UNIVERSITY OF WASHINGTON)—Contact: U/W School of Medicine, Div. of CME, SC-50, Seattle, WA98195; tel 206-543-1050.
VMMC (VIRGINIA MASON MEDICAL CENTER)—Contact: Linda Orgel, Division of Continuing Medical Education, Virginia Mason Medical Center, PO Box 900, Seattle, WA 98111; tel 206-340-2058.
WSMA Washington State Medical Association—Continuing Medical Education, 2033 Sixth Ave, Ste 1100, Seattle, WA 98121; tel 206-441-9762.

WYOMING

All courses meet the criteria for Category 1 of the Physician's Recognition Award of the AMA. To list AMA Category 1 CME courses here, send information at least two months in advance to the Medical Education Committee, Wyoming Medical Society, PO B ox 4009, Cheyenne, WY 82009; e-mail skeefe@wyomed.org; tel 307-634-2424; fax 307-632-1973.

June 16-18, 1999: Annual Meeting/Scientific Session: Wyoming Medical Society. Jackson Lake Lodge, Moran WY. Contact: Susie Wacker; PO Box 4009, Cheyenne, WY 82003; swacker@wyomed.org.

NOTICE

State Associations should send their CME listings in electronic format (e-mail, PC or Mac disks) for publication to:

Catherine Nancarrow, Editorial Manager,
WJM Western Journal of Medicine,
PO Box 7690, San Francisco, CA 94120-7690;
415-974-5977; fax 415-882-3379; wjmsf@pacbell.net.

Guidelines for Authors

Our readers represent all disciplines of medicine, but principally primary care physicians. We aim to publish manuscripts that are reliable and lively and that will improve the care of patients, the health of the public, or policies affecting either. Manuscripts should be of interest to a broad range of busy practitioners, physicians in training, and anyone who has an interest in quality health care. The purpose of a paper or letter may be to report, inform, alert, review, and discuss, but, above all, to teach. We aim to give quick and informative decisions on the articles we receive.

Manuscript submission information

Manuscripts should be sent to:
Managing Editor, Catherine Nancarrow,
WJM Western Journal of Medicine,
221 Main Street, PO Box 7690,
San Francisco, CA 94120-7690;
wjmsf@pacbell.net.

Manuscripts may be submitted via e-mail, but must include print mail address and phone and fax numbers of the correspondent.

Manuscripts must be original, not previously published, and not under consideration by another publisher. If preliminary data were included in another presentation or publication, this should be noted in the cover letter and a copy of that publication should be included.

Any conflict of interest, actual or potential, should be revealed to the Editors (see Letter of Transmittal). Research or project support should be included as a footnote to the manuscript and detailed in the Letter of Transmittal. Obtaining informed consent to protect patients' rights to privacy should be documented according to URM 1997.

All manuscripts should be double-spaced and, including references and abstract but not tables, should not exceed:

- **Original articles**: 2,500 words with a maximum of five tables and 30 references; structured abstract
- **Topics in Review**: 1,500 to 2,000 words with a maximum of 25 references; summary points†
- **Topics for Best Practice**: 2,000 words
- **Evidence-Based Case Reviews**: 2,500 words with two tables and/or figures; summary points†
- **Commentaries**: 600-800 words
- **Letters to the Editor**: 500 words

Structured abstracts

Manuscripts, except for case-based reviews, should include a structured abstract of no more than 250 words with the headings: objectives, design, setting, subjects, interventions, main outcome measures, results and conclusions.

Evidence-based case reviews

Interesting cases presented in an evidence-based, case-based review format provide readers with information and guidance with respect to clinically relevant choices made by practitioners—from diagnostic methods to conclusions as to what might have been done differently given the outcome. Topics to address include:

- epidemiology
- differences in demographic groups
- an evidence-based approach to diagnosis, management, and therapeutics; ethical issues
- cost/economic issues; when to involve a specialist
- what research is needed in the area.

Use of diagrams, tables, and algorithms is highly recommended. Authors should include 5-7 bulleted summary points for a busy primary care provider.

Letters to the editor

Letters must be double-spaced and will be published at the discretion of the Editors. They may be edited for style and brevity. Those of a scientific nature may be subject to peer review.

Letter of transmittal

All authors must sign the letter of transmittal, with one author designated as correspondent and his or her name, address, and telephone and fax numbers included.

A letter of transmittal, except for one accompanying a manuscript from US government employees whose work was done as part of their official duties, must include:

- a paragraph that **transfers copyright:** "In consideration for reviewing and editing my submission, the author(s) undersigned hereby transfers, assigns, or otherwise conveys all copyright ownership to *WJM Western Journal of Medicine,* in the event that such work is published by the journal."
- a statement of **author responsibility** signed by all authors: "I have participated in the conception and design of this work and in the writing of the manuscript and take public responsibility for it. I have reviewed the final version of the

manuscript and approve it for publication. I attest to the validity and legitimacy of data in the manuscript and agree to be named as the lead author or coauthor of the manuscript."

- a description of **sources of funding and the role of sponsors,** including their involvement, if any, in review and approval of the manuscript for publication.
- a statement of **financial disclosure:** "I warrant that I have no financial interest in the drugs, devices, or procedures described in the enclosed manuscript (except as disclosed in the attached statement)."
- a statement that all human subjects involved in experimental investigation gave their **informed consent** and that approval was obtained from the appropriate institutional review board.

Editorial review

All manuscripts are subject to peer review in addition to review by the Editors to determine the originality, validity, and importance of content and conclusions. *WJM* aims to introduce an open peer review system; reviewers' comments may be signed. Reviewers are required to state all possible conflicts of interest.

All accepted manuscripts are subject to copyediting. The corresponding author receives edited page proofs for approval and minor changes and is responsible for clearing all corrections and changes with coauthors.

Manuscript preparation

All manuscript materials, including references, tables, figure legends, and abstracts, must be double-spaced.

Please submit the following:

- The original manuscript, two copies, and a copy of the manuscript (including references, tables, and figure legends) on disk (formatted for a PC/Windows platform and labeled with the word processing program used). Allow a margin of 2.5 to 4 cm (1 to 1.5 in) on both sides.
- Figures, black and white or color, in triplicate unmounted 12.7 × 17.8 cm (5 × 7 in) glossy prints (and transparencies for color figures) with the figure number, lead author's name, and top of the photo indicated with a label on the back.

WJM encourages the use of illustrations and asks authors to submit photographs for publication. When possible, patients should be asked to sign consent forms before pictures of them are published. This should be clearly stated and proof submitted with the manuscript. If obtaining consent is not possible, the reason should be stated in the cover letter. Changing the data on patients should not be used as a way of securing anonymity.

Figure legends, to be typed in sequence on the same page, should be in complete sentences. A letter of permission to borrow from the copyright holder (the previous publisher) must accompany any figures or tables previously published. The permission of the authors should also be obtained. The Editors discourage the use of borrowed figures or tables.

Reprints

A form for ordering reprints will be sent to the corresponding author when the article is published.

References

All references should be cited in the text using superscript numbers and listed in their order of citation. Reference style should follow guidelines adopted by the US National Library of Medicine. The title of the article, name of publication, year of publication, volume number, and first and last page numbers should follow the authors' names.

Journal articles

Abbreviations of journal titles should conform to those used in Index Medicus. List up to six authors; for seven or more, use et al after listing the first six.

Vega KJ, Pina I, Krevsky B. Heart transplantation is associated with an increased risk for pancreatobiliary disease. *Ann Intern Med* 1996; 124:980-982.

Books

Ringsven MK, Bond D. *Gerontology and Leadership Skills for Nurses.* 2nd ed. Albany (NY): Delmar Publishers; 1996.

Personal communications and unpublished data

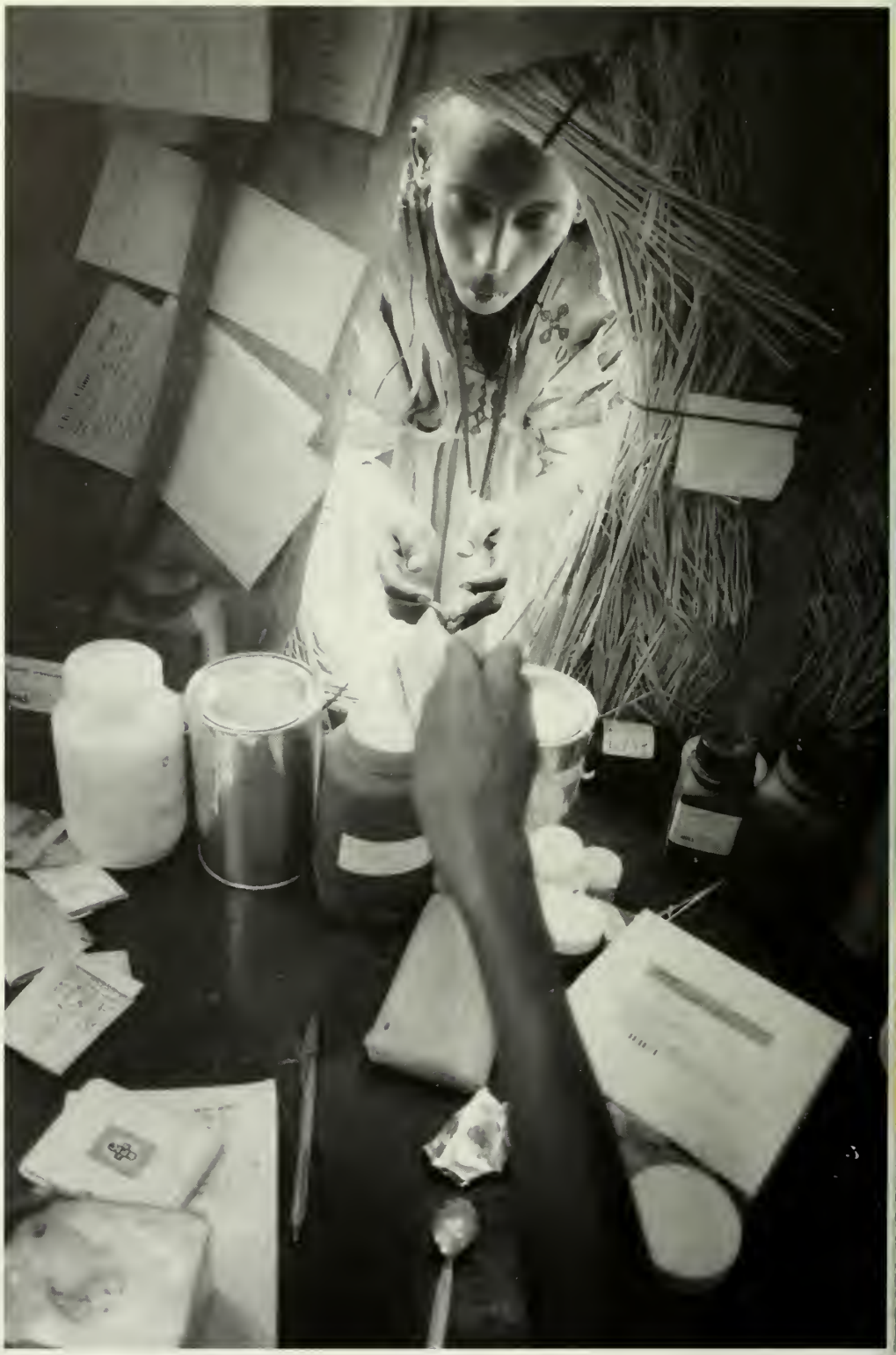
The use of "personal communication" or "unpublished data" should be avoided and should not be included in the reference list.

For further information

Questions regarding the Guidelines for Authors may be directed to the Managing Editor in writing at the address above or by telephone 415-974-5977, fax 415-882-3379, or e-mail (wjmsf@pacbell.net).

Author checklist

- Original double-spaced manuscript and two copies, as well as PC-formatted disk.
- Illustrations, glossies and/or transparencies, identified with lead author's name, plus figure legends that describe fully and in complete sentences what the figure depicts.
- Letter of transmittal that includes release of copyright, statement of conflict of interest, funding source(s), and authorship responsibility, signed by all the authors.
- A 250-word structured abstract.
- Title page that includes current affiliation of all authors and all contact details for the corresponding author (street and e-mail addresses, phone numbers, fax numbers).
- Permission-to-borrow letters for any previously published illustrations or tables.
- Informed consent obtained.



Pharmacy, Fau 3 Refugee Camp, Eastern Sudan, March 1985.

David Heiden

Drought affected the entire Sahel region of Africa between 1984 and 1985, but in Ethiopia the humanitarian crisis was made particularly severe by the civil war. During this time 350,000 people from the Tigre province of Ethiopia sought refuge in Sudan and were housed in 37 camps set up along the Sudan-Ethiopian border.

Fau 3 was one of those camps established in February 1985 and abandoned in April 1987 when the refugees from Tigre returned home. About 12,500 people were initially placed there and during the first few weeks the death rate was as high as 15 people per 10,000 per day.

About the artist In a world's record example of dawdling, I didn't complete my last training program until 25 years after starting medical school. I went through residencies in internal medicine and ophthalmology, fellowships in cardiovascular disease, blood coagulation, and uveitis, and spent a dozen years as an emergency room doctor. In hospitals and clinics in New York City and San Francisco I learned wonderful skills.

But a different education began on the Cambodian border and continued in refugee camps in Somalia and Sudan, during emergency immunization in Uganda in the aftermath of Idi Amin, in the National Leprosy Hospital in Yemen and finally in India and Tibet. Far from the familiar lecture halls and wards of American teaching hospitals, I began to appreciate how medicine reflects the values of any society, sometimes to the extent that fundamental issues of purpose get lost. I got a better sense of the things that made a doctor important before there were antibiotics and gene therapy.

I always kept a diary and I compulsively took pictures. Some of the pictures were published in a book, *Dust to Dust, a Doctor's Experience of African Famine* (Temple University Press, 1992), and the collected experience is now being shaped into another book, which will be completed once the demands of a busy practice and raising small children diminish.

David Heiden is an ophthalmologist practicing in San Francisco.

NEW IN 1999

Clinical Evidence

from ACP-ASIM and BMJ Publishing Group

Clinical Evidence is a compendium of evidence on the benefits and harms of common clinical interventions. Written by practising clinicians using rigorous searching and evaluation methods, it will be issued every six months to bring you the most reliable and up-to-date findings on important questions in clinical practice. *Clinical Evidence* will be published as a convenient reference book in order to make clinical effectiveness accessible and possible for health professionals worldwide.

Clinical Evidence will enable clinicians and health care professionals to make informed decisions about:

- Choosing one treatment or test over another
- Informing patients and their families, and involving them in decision making
- Identifying gaps in the evidence
- Conducting and commissioning research
- Auditing clinical procedures
- Resolving disputes over efficacy of treatment
- Training clinicians, managers and students

The first issue will contain:

- Breast Diseases
- Cardiovascular Diseases
- Child Health
- Diabetes
- Digestive System Diseases
- Diseases of Ear, Nose & Throat
- Eye Diseases
- Gynaecological Disorders
- Infectious Diseases
- Mental Health
- Musculoskeletal Diseases
- Neurological Diseases
- Respiratory Diseases
- Wounds
- Skin Diseases
- Sexual Health
- Urinary Tract Disorders

blished in convenient reference format for ease of e, Clinical Evidence is available by subscription in and UK editions.
ample section of Clinical Evidence is available for to view on the web at: www.evidence.org.
bscribing couldn't be easier, simply complete the er form below and return with payment to the dress provided.

nical Evidence
99 Subscription rates - Regular rate: US$99
P-ASIM member rate: $89 Institutional rate: $192
stitutional rate applies to any library or organisation buying for the use of re than one person)
dent rate: US$53 (Students please provide proof of student status)
blication: Six monthly

ase tick which edition you would like to receive)
US edition (first issue available October 1999)
UK edition (first issue available June 1999)

ase tick:
I enclose a check for $ .....
(Payable to British Medical Journal. US dollar checks to be drawn on a USA bank account)
Charge my credit card £ .....
American Express / Visa / MasterCard / Delta
dholders No
☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐

iry Date:.....Signature: .....

Name:.....

Job title: .....

Address:.....

.....

Country: .....Postcode: .....

E-mail Address: .....

☐ Please tick if you do not wish your data to be used for direct marketing purposes

Return to: BMJ Publishing Group, Box 590A, Kennebunkport, ME 04046, USA
Tel: 1-800-2-FON-BMJ Fax: 1-800-2-FAX-BMJ
Email: bjpaige@cybertours.com

N.B. Subscribers in Canada must add 7% GST to the quoted dollar price unless they can provide a registration number

Visit our website at: www.evidence.org

BMJ Publishing Group

A C P
ASIM

Specialist Journals from BMJ Publishing Group

Live and Online

Now on a screen near you

- Free until July 1999
- Full text
- Fully searchable archive
- Articles collected by topic
- Customised email alerts
- Direct Access to Medline

eHEART www.heartjnl.com NOW ONLINE

eJNNP www.jnnp.com NOW ONLINE

eBJO www.bjophthalmol.com NOW ONLINE

eGut www.gutjnl.com NOW ONLINE

eThorax www.thoraxjnl.com NOW ONLINE

eARD www.annrheumdis.com NOW ONLINE

eADC www.archdischild.com NOW ONLINE

BMJ Publishing Group

wjm
western journal of medicine
Volume 170 Number 6 June 1999

DISPLAY SHELVES

Hepatitis A: should we immunize all children?

Doctors without Borders talks about Kosovo

Why peyote is more than a natural high

Full text, free access.

– Fully searchable archive –

– 150 topic collections –

– Customised email alerting –

– Rapid responses –

– Enhanced articles –

– Extra news stories –

– Direct Medline access –

– Jobs, courses, and careers –

And we don't ask you to pay, subscribe, register, provide passwords, or fill in interminable online questionnaires.

www.bmj.com

This month in wjm

Guidelines must be based on evidence to avoid bias and self interest

Guidelines don't always improve patient treatment, often because they're never implemented. They may not be implemented because physicians feel their views haven't been represented in drawing up the guidelines. On p.348, Paul G. Shekelle and colleagues explain how to draw up guidelines by setting up development groups, assessing and then interpreting the evidence from systematic reviews, and finally, getting the guidelines externally reviewed. They warn that conclusive evidence exists for only a few things. In his commentary on p.352, Scott Weingarten argues that the effects of guidelines on patient care must be studied, so we can learn the most cost-effective way to develop them.

Patients dread having a sexual physical

It can be hard enough for patients to discuss their sexual problems with their physicians, but having their genitalia examined may be too embarrassing for them to contemplate. John Dean explains, however (p.364), the embarrassment can be reduced by warning patients exactly what the exam entails and how it might help them. Privacy, warmth, and an unhurried approach are all essential, as is a chaperone. It's important to look for signs of concomitant disease, such as cardiovascular, respiratory, and neurological illnesses that can cause sexual problems.

How to rate health information on the web

Many people surf the Web for health information, and while some of what they read is accurate, other sites may be misleading. Organizations frequently publish criteria on how to evaluate health information on the Web, but on p.329 Paul Kim et al find that out of 29 published rating tools, only 1 mentions confidentiality. This is worrying because many health sites collect personal health information to help develop their content. Sites also often fail to disclose who is financing them. On p.332, Kevin Patrick describes how patients use the Web for second opinions and says they must be able to assess the quality of the information available.

Reporting elder abuse may cause harm as well as doing good

Up to 2.5 million older people in the United States are abused annually, warns Calvin H. Hirsch on p.353. They may be neglected, physically or emotionally abused, or financially exploited. Many of them will present to physicians because of the physical consequences of being abused, but often doctors miss the signs and attribute their distress to old age. Over 40 states require health care workers to report suspected elder abuse, and while such mandatory reporting can save the lives of older people, it may sometimes escalate the abuse. Families are best approached in a non-confrontational way and helped by multidisciplinary teams, based in the community.

Medicine should resuscitate the use of narrative

Too often a clinical clerking involves reeling off a list of questions and scribbling down the answers without listening to them. By doing so, physicians may miss what's significant to their patients and make them feel helpless. On p.367, Trisha Greenhalgh suggests that we need to regain the skills of listening to, appreciating, and interpreting patients' stories. These abilities, rather than being unscientific and unstructured, are core clinical skills that encourage empathy and can improve clinical outcomes for patients.

Wanted: medicine man

Traditional healers have a special place in their communities. Their therapies combine ritual and participation by their patients' neighbors and family. In "Letter from the Southwest" (p.384) Mark Carroll describes his idea to employ a medicine man in a weekly clinic in a remote Navajo community. It took a healer to explain why you can't juxtapose conventional medicine and traditional therapy.

Should children be routinely vaccinated against hepatitis A?

Public health attempts have failed to control hepatitis A and 11 Western states have annual rates that are at least twice the national average. The Advisory Committee on Immunization Practices recommended earlier this year that all children in Western states should be vaccinated against the disease, a move that Chinh Le (p.324) welcomes. Le argues that targeting high-risk populations and trying to control outbreaks does not work, while vaccination is cost effective and should also be encouraged in susceptible adults. On p.325, John Takayama warns that numerous questions need to be answered before universal childhood immunization goes ahead and that children and parents may react badly to the "pin-cushion" effect.

wjm

wjm western journal of medicine

221 Main Street, PO Box 7690, San Francisco, California 94120-7690

Co-editors:
Michael S Wilkes, Los Angeles, CA
mwilkes@ucla.edu

Miriam Shuchman, Buffalo, NY
shuchman@acsu.buffalo.edu

Deputy Editor:
Luisa Dillner, London, UK
ldillner@bmj.com

Editorial Manager:
Catherine Nancarrow
wjmsf@pacbell.net
Tel 415-974-5977
Fax 415-882-3379

Business & Marketing Manager:
Ruth Staunton
rstaunton@bmjgroup.com
Tel 415-974-1071
Fax 415-882-3379

Production Manager
Neil Poppmacher, London, UK

Picture Researcher
Jan Croot, London, UK

Technical Editor
Miriam Pinchuk, London, UK

Associate Editors:
David Grossman, Seattle, WA
Jerome Hoffman, Los Angeles, CA
Richard Kravitz, Davis, CA
John Takayama, San Francisco, CA

Section Editors

Medical Humanities
Janice L Willms, Santa Barbara, CA

Med.Pix
Richard Usatine, Los Angeles, CA

Evidence-Based Medicine
Nathan Link, New York, NY

Cultural Medicine
Geri Ann Galanti, Los Angeles, CA

eWJM
Doug Bell, Los Angeles, CA
Mark Granoff, Los Angeles, CA

Editorial Advisors
Elaine Batchlor, Oakland, CA
Joel Braslow, Los Angeles, CA
David Carlisle, Los Angeles, CA
Linda Clever, San Francisco, CA
Mitch Feldman, San Francisco, CA
Lillian Gelberg, Los Angeles, CA
Jan Gurley, San Francisco, CA
Seth Landefeld, San Francisco, CA
Gina Moreno-John, San Francisco, CA
Stephen McPhee, San Francisco, CA
Sylvia Ramos, Albuquerque, NM
Peter Rudd, Palo Alto, CA
Robert Tibshirani, Palo Alto, CA
Jeffrey Tice, San Francisco, CA
Howard Waitzkin, Albuquerque, NM
Mary White, San Francisco, CA

Editorial Board
Ann Alpers, San Francisco, CA
Margaret Battin, Salt Lake City, UT
Marshall Block, Phoenix, AZ
William A Boehm, Alamogordo, NM
Rubin Bressler, Tucson, AZ
Robert Brook, Los Angeles, CA
Haile T Debas, San Francisco, CA
Thomas DeCoster, Albuquerque, NM
Albert Deisseroth, Houston, TX
Sandy Feldman, La Jolla, CA
Alan Fogelman, Los Angeles, CA
ERW Fox, Coeur D'Alene, ID
J Christian Gillin, San Diego, CA
Gary Glazer, Stanford, CA
John Greenlee, Salt Lake City, UT
John H Holbrook, Salt Lake City, UT
Vince Iacopino, Las Vegas, NV
Lewis Judd, La Jolla, CA
Norman Kahn, Kansas City, MO
Carol Lake, Sacramento, CA
Alex G Little, Las Vegas, NV
Jerold M Lowenstein, San Francisco, CA
Joseph L Lyon, Salt Lake City, UT
Julie G Madorsky, Pomona, CA
Michael L Manco-Johnson, Denver, CO
Daniel Mishell Jr, Los Angeles, CA
Albert A Moss, Seattle, WA
Thomas E Norris, Seattle, WA
George A Ojemann, Seattle, WA
Linda Rosenstock, Washington, DC
Paul Rousseau, Phoenix, AZ
Irwin J Schatz, Honolulu, Hawaii
Joe Schoeber, Casper, WY
Joe Selby, Oakland, CA
David Shander, Denver, CO
Martin Shapiro, Los Angeles, CA
Linda Shortliffe, Stanford, CA
Norman E Shumway, Stanford, CA
Gregory Simon, Seattle, WA
Anthony So, New York, NY
Robert Strickland, Albuquerque, NM
Diane Wara, San Francisco, CA
Stephen I Wasserman, San Diego, CA
Ronald Weinstein, Tucson, AZ
Clifton R White Jr, Portland, OR
Leslie Wiener, Los Angeles, CA
Charles Wilson, San Francisco, CA

Submitting manuscripts
Send manuscripts to Catherine Nancarrow at the above address. Guidelines for Authors available on request.

Subscriptions
Contact Jennifer Paige
WJM, Box 590A,
Kennebunkport ME 04046;
tel 800-236-6265; fax 800-232-9265
e-mail bjpaige@cybertours.com

1999 Subscription rates:
Regular $70 US/Canada; $85 Other
Institutional $120 US/Canada; $130 Other
Student, Group and Association rates available on request
Single copies $15 US/Canada

Display advertising and reprints
Contact Marsha Fogler
Medical Reprint Services,
PO Box 3227,
Cherry Hill, NJ 08034;
tel 800-482-1450; fax 609-482-7414
e-mail fogler@erols.com

Advertisements: Artwork for display advertising must be received no later than the first of the month preceding issue. Advertising rates will be sent on request. Acceptance of advertising is contingent upon approval by the Publisher. WJM reserves the right to refuse any advertisement.

Classified advertising
Contact Ruth Staunton at WJM,
tel 415-974-1071; fax 415-882-3379;
e-mail rstaunton@bmjgroup.com

WJM Western Journal of Medicine
(ISSN 0093 0415/USPS 084 480)
is published monthly by BMJ Publishing Inc., 221 Main Street, PO Box 7690, San Francisco, CA 94120-7690. Copyright © BMJ Publishing Inc. 1999. All Rights Reserved. Periodicals postage paid at San Francisco, CA and additional mailing offices.

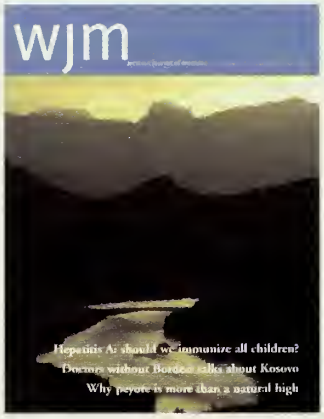
POSTMASTER
Send address changes to WJM, PO Box 590A, Kennebunkport, ME 04046-9801

BMJ Publishing Group

UCSF STANFORD HEALTH CARE

WJM is owned by BMJ Publishing Group and UCSF Stanford Health Care.

WJM is the official journal of the following medical associations: Alaska, Arizona, California, Denver, Idaho, Nevada, New Mexico, Utah, Washington, and Wyoming


wjm
Hepatitis A: should we immunize all children?
Doctors without Borders talks about Kosovo
Why peyote is more than a natural high

June 1999

Big Bend of Texas with Rio Grande River–natural habitat of peyote.
Robert & Linda Mitchell

321 This Month in *WJM*

Op-Ed

324 Control of hepatitis A infection in the United States
Chinh Le

325 Universal childhood immunization against hepatitis A: whoa!
John I Takayama

326 Managing/understanding chronic disease: a call for papers
Michael S Wilkes, Miriam Shuchman

Mail

328 Fatal peyote ingestion associated with Mallory-Weiss lacerations
Kurt B Nolte, Ross E Zumwalt

Original Research

329 Review of published criteria for evaluating health-related Web sites
Paul Kim, Thomas Eng, Mary Jo Deering, Andrew Maxfield

332 Commentary
Kevin Patrick

Med.Pix

334 A rash on the feet and buttocks
Richard P Usatine

Research Digest

336 A brief smoking cessation intervention for adults in hospital is cost-effective
RT Meenan, VJ Stevens, MC Hornbrook, et al

336 Commentary
Patricia W Stone

THE FRANCIS A. COUNTWAY
LIBRARY OF MEDICINE
BOSTON, MA

OCT 25 1999

contents wjm

Volume 170 Number 6 JUNE 1999

337 Learning how to live with a child with ADHD is a long process
J Kendall

337 Commentary
Steven Pryjmachuk

338 Women develop multiple coping strategies to deal with menopausal transitions
LA Kittell, P Kernoff Mansfield, AM Voda

338 Commentary
Debbie Kralik

Best Practice

339 Evidence-Based Case Review
Heart failure: Part II.
Michael S Wilkes, Holly Middlekauf, Jerome R Hoffman

343 Clinical Evidence
Genital herpes
Anna Wald

348 Developing clinical guidelines
Paul G Shekelle, Steven H Woolf, Martin Eccles, Jeremy Grimshaw

352 Commentary
Scott Weingarten

353 Topic in Review
The primary care of elder mistreatment
Calvin H Hirsch, Sara Stratton, Roberta Loewy

359 Medicine Cabinet
Quinolones: which generation for which microbe?
Meganne S Kanatani, Monica K Lee

362 Curbside Consult
Do growing pains exist?
AW Craft

363 What is a stitch?
Gerry Haggerty

364 Toolbox
How to do a sexual physical exam
John Dean

Culture and Medicine

367 Why study narrative?
Trisha Greenhalgh, Brian Hurwitz

370 *WJM* interview with Dr. James Orbinski
Miriam Shuchman

Photograph courtesy of Medecins Sans Frontieres

In the Public Eye

373 Media Watch
The kidney dilemma
Deborah Josefson

375 News and Features

378 Medicine and Money
Why HMOs are dumping their Medicaid patients
Scott Gottlieb

379 Commentary
Elaine Batchlor, Crystal Hayling

West of the Rockies

382 Speaker's Corner
Unnerving: a patient's view of the debate over prostate cancer
William J Drummond

383 Mass immunization, Uganda, 1983
David Heiden

384 Letter from the Southwest
A medicine man and a lesson learned
Mark Carroll

385 Classified Ads

386 CME Announcements

390 Guidelines for Authors

392 Visual Commentary
David Heiden

Correction: on p.274 of the May issue the e-mail for Dr. Lisa Chew was incorrect. The correct address is lchew@washington.edu.

Op-Ed

Control of hepatitis A infection in the U.S.

Vaccination against hepatitis A is cost-effective and safe for children in high risk states

Chinh Le

Infectious Disease Specialty
Kaiser Permanente
Medical Group, Inc.
Northern California
Division
Chinh.Le@kp.org

Conflicts of interest:
Opinions expressed are Dr. Le's, not of Kaiser Medical Permanente Medical Group, Inc. or the ACIP/CDC. Dr. Le is a stockholder with Merck Pharmaceutical Co.

The control of hepatitis A has been elusive, despite the licensure of the Hepatitis A vaccine in 1995 and the recommendations by the Advisory Committee on Immunization Practices (ACIP) for immunization of "high risk individuals" and for prevention in populations with very high rates of disease.[1] The national incidence rate has remained constant at 10 to 15 reported cases per 100,000 population between 1976 to 1997, with wide variations and a diverse and complex epidemiology between states or counties within a state.[2] Eleven western states (Arizona, Alabama, Oregon, New Mexico, Utah, Washington, Oklahoma, South Dakota, Nevada, California, and Idaho) had the unfortunate distinction of having annual rates from 20 to 40/100,000 in the last decade.

In geographically or ethnically well-defined populations with high rates of infection, such as American Indian reservations, Alaskan natives, or selected religious communities, routine vaccination of children, achieving 50% to 80% first dose coverage has controlled hepatitis A epidemics.[3,4] Vaccination programs to control outbreaks in communities[5] or specific high risk groups[6] have, however, been costly and difficult to implement, have achieved low vaccine coverage, and have had an uncertain impact on preventing future outbreaks. The estimated annual direct and indirect cost of hepatitis A in 1989 was greater than $200 million.

It is not hard to understand that a strategy targeted at "high risk individuals" and focusing on controlling outbreaks will not achieve a sustained reduction of disease incidence. Large, common-source food outbreaks receive considerable public attention but contribute less than 5% of reported cases. Approximately 50% of cases have "unknown" source or risk factors, presumably person-to-person spread, predominantly from children and young adults. Community outbreak investigations have revealed very complex and diverse demographic factors, including, in some western and midwestern states, the association with illicit drug use, especially amphetamines.

The recent ACIP recommendation for routine childhood hepatitis A vaccination in states where the average annual incidence during 1987-1997 was at least 20/100,000 population (i.e., double the national average) represents a shift in the overall strategy from outbreak control to a stepwise effort in achieving universal immunization of the U.S. population. Mohtashemi and colleagues from the Centers for Disease Control and Prevention estimated that routine infant immunization would result in a 99% reduction of hepatitis A in the U.S. in 3 to 10 years, depending on the vaccination rate and other factors.[7] Preliminary calculations by Meltzer and Bell (CDC, unpublished data) estimated that the cost of universal childhood immunization against hepatitis A would be comparable to other programs such as varicella and rotavirus immunizations.

Concern has been raised about public and providers' acceptance of another vaccine in the already loaded childhood immunization schedule and the ability of public health and other insurers to pay for a new vaccine program. Vaccination against hepatitis A, however, is likely to be widely accepted by parents because of the safety of the vaccine[8] and the public perception that this is a highly contagious and morbid disease. Funding will come with the Vaccine for Children Program (VFC) and as state legislatures and insurers realize the potential cost-benefits of the vaccination. Although more studies are needed to establish the duration of protective efficacy, there are epidemiologic and immunologic data supporting the use of a single dose schedule[3,4,9] with further reduction in the cost of mass immunization. A combined vaccine against hepatitis A and B has been shown to be safe and efficacious in individuals older than 1 year of age.[10] It is licensed for use throughout Europe and other countries and may be ideal for catch-up immunization of those who need immunization against both diseases. Although an infant formulation is not yet available, there is no reason not to start both the hepatitis A vaccine program with 2-year-old children and catch-up immunization of older children. Finally, since the morbidity and mortality (0.3% to 1.8%) of hepatitis A is much higher in adults than in children, a case can also be made to encourage immunization of susceptible adults living in endemic areas in the U.S.

References

1. Centers for Disease Control and Prevention. Prevention of hepatitis A through active or passive immunization. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 1996; 45(RR-15):1-30.
2. Bell BP, Shapiro CN, Alter MJ, et al. The diverse patterns of hepatitis A epidemiology in the United States – Implications for vaccination strategies. *J Infect Dis* 1998; 178:1579-84.
3. Werzenberger A, Mensch B, Kuter B, et al. A controlled trial of a formalin-inactivated hepatitis A vaccine in healthy children. *N Engl J Med* 1992; 327:453-7.
4. McMahon BJ, Beller M, Williams J, et al. A program to control an outbreak of hepatitis A in Alaska by using an inactivated hepatitis A vaccine. *Arch Pediatr Adolesc Med* 1996; 150:733-9.
5. Craig AS, Sockwell DC, Schaffner W, et al. Use of hepatitis A vaccine in a community-wide outbreak of hepatitis A. *Clin Infect Dis* 1998; 27:531-5.
6. Centers for Disease Control and Prevention: Hepatitis A vaccination of men who have sex with men – Atlanta, Georgia, 1996-1997. *MMWR* 1998; 47(No. 34):708-11.
7. Mohtashemi M, Coleman PJ, Mast EE, et al. Theoretical epidemiologic effects of routine childhood hepatitis A vaccination in the United States. Presented at the International Conference on Emerging Infectious Diseases, March 8-11, 1998. Atlanta, GA.
8. Niu TM, Salive M, Krueger C, et al. Two-year review of hepatitis A vaccine safety: Data from the Vaccine Adverse Event Reporting System (VAERS). *Clin Infect Dis* 1998; 26:1475-6.
9. Werzberger A, Kuter B, Nalin D. Six years' follow-up after Hepatitis A vaccination. *N Engl J Med* 1998; 338:1160.
10. Diaz-Mitoma F, Law B, Parsons J. A combined vaccine against hepatitis A and B in children and adolescents. *Pediatr Infect Dis J* 1999; 18:109-14.

Universal childhood immunization against hepatitis A: whoa!

Numerous questions should be answered first

John I Takayama
Division of General Pediatrics, Department of Pediatrics
Campus Box 0503, UC San Francisco, San Francisco, CA 94143
jtaka@itsa.ucsf.edu

In February of 1999, the Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control and Prevention (CDC), recommended that the hepatitis A vaccine be provided to all children in the western United States.[1,2] Past strategies of outbreak control had not resulted in lowered rates of hepatitis A.

Although routine immunization has been an effective public health intervention for lowering disease incidence in populations, it is important to understand the evidence for and implications of such a policy. Several aspects of this disease and its prevention must be considered: its unique epidemiology and its differential impact on patients by age; the long-term efficacy and side effects of the vaccine; its incorporation into an already crowded childhood vaccination schedule; and its acceptance by parents and health care providers.

Furthermore, relatively rare side-effects may become significant when the vaccine is administered to a much larger population.

Hepatitis A does not affect all communities uniformly. The ACIP defines "high-rate" communities with widespread infection and acquisition of nearly universal immunity to hepatitis A by young adulthood; these consist of distinct racial or ethnic groups, such as American Indians and Alaskan Natives, as well as some religious communities.[3] Although the source for nearly half of clinical cases reported to the CDC in 1990-1992 was unknown, a personal contact was identified in 24%, a child care center in 15%, international travel in 6%, food- or water-borne outbreaks in 4%, male homosexual contact in 4%, and injected drug misuse in 3%.[4] Regional variability has been shown in a recently published study of four sentinel counties in which injecting street drugs was a major factor, associated with 14% of cases overall and 22% in Pierce County, Washington.[5] The recently publicized reports of the high incidences of hepatitis A in the western states, however, do not discuss the extent of contribution of any of these factors. If hepatitis A is limited to distinct populations, why immunize everyone?

Approximately 30,000 cases of hepatitis A are reported every year, and this is likely to be an underestimate.[6] Although the incidence is higher among infants and preschool-aged children, adults and especially the elderly bear the brunt of morbidity and mortality. In an outbreak in Tennessee in 1994 and 1995, 1700 cases were reported, 256 patients hospitalized, 35 patients had complications, and 5 died. A quarter of patients 40 years or older had at least one complication compared to 11% of patients younger than 40. All deaths were among adults.[7]

Although fecal-oral spread from asymptomatic infections, particularly from young children, may account for a high proportion of hepatitis A virus spread, in contrast to the array of diseases for which universal childhood immunization has been recently recommended (such as *Haemophilus influenzae* type b, hepatitis B, rotavirus and even varicella), hepatitis A is mostly an acute self-limited illness with few or mild symptoms among children. How should we interpret the rationale of immunizing children against a disease that is significantly more symptomatic and serious among adults?

Although the notion of a captive population and the difficulty of assuring immunization compliance among adults have been cited, are there ethical considerations? Might universal immunization absolve societal responsibilities to improve health care for at-risk populations?

Children, parents, and health care providers have experienced a recent rise in the number of required vaccines (including injections) routinely administered during early childhood. In the first 2 years of life, children receive up to 16 injections comprised of varying combinations of vaccines against diphtheria, tetanus, pertussis, polio, *Haemophilus influenzae* type b, hepatitis B, measles, mumps, rubella, varicella, and rotavirus. Since the currently available vaccines against hepatitis A, HAVRIX (SmithKline Beecham) and VAQTA (Merck and Co.), are not approved for children younger than 2 years, 2 additional injections would be needed. How will children, parents, and health professionals react to the "pin-cushion" phenomenon? Might overall rates of immunization against childhood diseases be affected? Will the current recommendation influence the acceptance of subsequent vaccines slated for recommendation, such as the pneumococcal vaccine? (*Pneumococcus* is currently the most important organism causing meningitis in infants and children.)

The hepatitis A vaccine is effective in children for at least 5 years, and a longer duration of protection is predicted.[8] A recent 2-year surveillance has shown few significant adverse events.[9] How the developing human body responds long-term to additional introductions of multiple foreign antigens remains unclear.[10] Furthermore, relatively rare side-effects[11] may become significant when the vaccine is administered to a much larger population. The cost of 1 dose of the vaccine is $22.80; any recommendation for universal immunization, therefore, must address reimbursement. If it is included in Vaccine For Children (VFC), a national program that provides vaccines free-of-charge to those who are uninsured or have public insurance, this may help to assure the nondisparate distribution of the vaccine, especially given higher rates of hepatitis A among low-income, immigrant, and traditionally underserved children.

The ACIP may have hastened its announcement of universal childhood immunization against hepatitis A. Numerous questions need to be answered before states, providers, and families embrace such unilateral recommendations.

References:
1. Tucker ME. Geography key in vaccine guidelines. *Pediatric News* 1999; 33:1,5.
2. Richards CA. Hepatitis A vaccination recommended for children living in high-risk areas. *Infectious Diseases in Children* 1999; 12:8.
3. Centers for Disease Control and Prevention. Prevention of hepatitis A through active or passive immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Morbidity and Mortality Weekly Report* 1996; 45(RR-15):1-30.
4. American Academy of Pediatrics. Hepatitis A. In: Peter G, ed. *1997 Red Book: Report of the Committee on Infectious Diseases,* 24th ed. Elk Grove Village, IL: American Academy of Pediatrics; 1997:237.
5. Bell BP, Shapiro CN, Alter MJ, Moyer LA, Judson FN, Mottram K, Fleenor M, Ryder PL, Margolis HS. The diverse patterns of hepatitis A epidemiology in the United States—implications for vaccination strategies. *J Infectious Disease* 1998; 178:1579-84.
6. Centers for Disease Control and Prevention. Summary of notifiable diseases, United States, 1995. *MMWR Morbidity and Mortality Weekly Report* 1996; 44:6.
7. Willner IR, Uhl MD, Howard SC, Williams EQ, Riely CA, Waters B. Serious hepatitis A: an analysis of patients hospitalized during an urban epidemic in the United States. *Ann Intern Med* 1998; 128:111-4.
8. Fan PC, Chang MH, Lee PI, Safary A, Lee CY. Follow-up immunogenicity of an inactivated hepatitis A virus vaccine in healthy children: results after 5 years. *Vaccine* 1998; 16:232-5.
9. Niu MT, Salive M, Krueger C, Ellenberg SS. Two-year review of hepatitis A vaccine safety: data from the Vaccine Adverse Event Reporting System (VAERS). *Clinical infectious diseases* 1998; 26:1476-7.
10. Passmore SJ, Draper G, Brownbill P, Kroll M. Case-control studies of relation between childhood cancer and neonatal vitamin K administration. *BMJ* 1998; 316:178-84.
11. Ferrazzi V, Jorgensen C, Sany J. Inflammatory joint disease after immunizations: a report of two cases. *Revue du Rhumatisme.* English Edition, 1997; 64:227-32.

Managing/understanding chronic disease: a call for papers

Chronic disease dominates medical practice but patients don't always get the best care

Michael S Wilkes
Miriam Shuchman
Co-Editors, *WJM*

Rapid improvements in health and longevity are dramatically changing the burden of illness throughout the world. In developed countries, changes in lifestyle and improvements in the treatment of major causes of mortality have aged the population and increased the prevalence of chronic diseases. Poor countries that have achieved gains in life expectancy are also experiencing an increase in chronic disease, as they proceed through the "epidemiological transition"—the changing pattern of health in which they inherit the problems of the rich.[1]

The epidemiological transition (now called the "health transition") has progressed substantially in several developing regions. This is demonstrated clearly in data on disability-adjusted life years (DALYs)—the sum of the number of years lost from premature death and the years lived with a disability.[2] The figure shows the ratio of DALYs caused by noncommunicable diseases to DALYs caused by communicable, maternal, perinatal, and nutritional conditions for the different regions of the world (Figure 1).

Thus most countries of the world are suffering from, or will soon suffer from, an enormous burden of chronic, noncommunicable disease. A few statistics illuminate the burden.[3] An estimated 691 million people in the world have high blood pressure. The number of diabetics worldwide is projected to increase from 135 million now to 300 million by 2025. An estimated 29 million people suffer from dementia, and 2.6 million new cases occurred in 1996. Rheumatoid arthritis affects about 165 million people.

Obviously the prevention of chronic disease through avoidance of risk factors is our first goal. Early detection and cure (when possible) is our second preference. But those objectives are often not met, and thus countries

and their health systems need to address the challenge of managing the chronic conditions that are becoming increasingly prevalent in our populations. To focus attention in this area, *WJM* will devote a special issue to chronic disease management in February 2000.

In the United States, the management of older and chronically ill patients increasingly dominates medical practice. Yet study after study, along with relevant performance indicators,[4] show that patients often miss out on effective pharmacological and behavioral therapies and lack the information and support they need. Many subspecialists argue that generalists do not provide high-quality care for people with chronic illness. Employers and health insurers are hiring disease management companies whose programs may "carve out" particular patients and conditions for separate care, threatening the integrity and continuity of the doctor-patient relationship. Practice system changes that have shown the greatest promise of success integrate self-management support programs, guideline-based treatment plans, nurse case management, more intensive follow-up, and registries that provide reminders and feedback.[5]

We hope *WJM's* theme issue on managing chronic disease will help disseminate research findings, encourage more research, and stimulate wider debate. In particular we invite authors to send us papers on the following topics:

- Clinical management of specific chronic conditions (such as asthma, diabetes, and HIV);
- Care of patients with multiple chronic conditions and the frail elderly;
- Practice-based interventions that address chronic disease care (e.g., informatics strategies, patient education);
- System-level strategies to improve the delivery of care for chronic illness (i.e., policies and programs implemented at the level of the health care delivery system);
- Disease prevention and risk reduction in persons with chronic illness;
- The integration of chronic disease management into primary care.

The editors do not wish to adhere to a rigid definition of "chronic disease" in considering papers for publication in these special issues. However, potential contributors who desire some guidance as to the meaning of the term may take note of the U.S. Centers for Disease Control and Prevention's definition: "illnesses that are prolonged, do not resolve spontaneously, and are rarely cured completely."[6]

WJM will publish a theme issue contemporaneously with the *BMJ's* special issue on the same topic. All manuscripts submitted to *WJM* will go through the usual peer review process. We ask authors to indicate their interest in having their accepted manuscripts published in *WJM* and in the *BMJ*. We are happy to consider reports from any part of the world and will welcome original research papers, editorials, educational articles, debate pieces, and rigorous review articles. The deadline for submission is August 1, 1999.

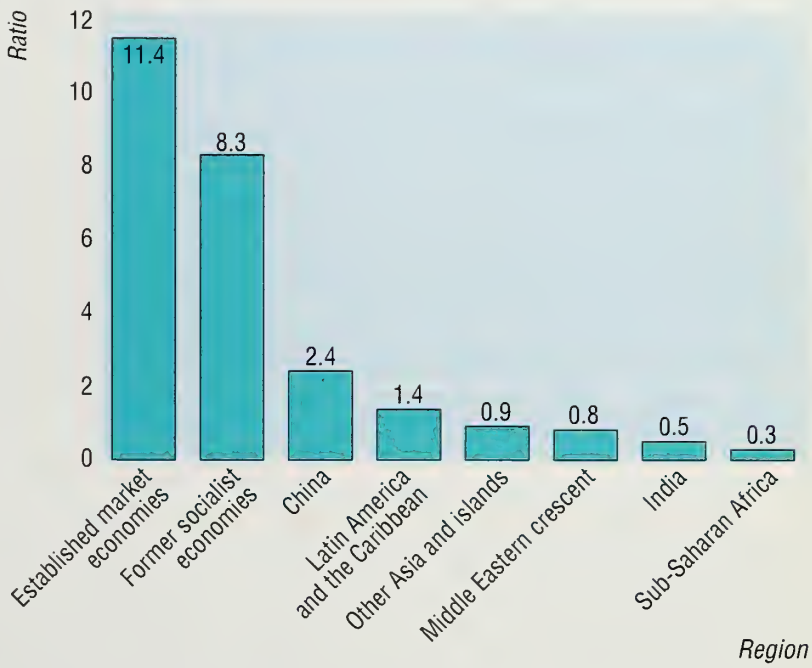


Figure 1 *Ratio of disability-adjusted life years (DALYs) caused by noncommunicable diseases to DALYs caused by communicable, maternal, perinatal, and nutritional conditions for the different regions of the world, 1990.*[2]

References

1. World Health Organization. *The world health report 1997: conquering suffering, enriching humanity.* Geneva: World Health Organization, 1997.
2. Harvard School of Public Health, World Bank, and World Health Organization. *The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected to 2020.* Murray CJL, Lopez AD, eds. Boston, Massachusetts: Harvard University Press, 1996.
3. Fifty facts from the World Health Report 1997. www.who.org/whr/1997/factse.htm (accessed 27 March 1998).
4. National Committee for Quality Assurance. NCQA's state of managed care quality report—1998. Washington, DC: National Committee for Quality Assurance, 1998. www.ncqa.org/pages/communications/state%20of%20managed%20care/report98.htm (accessed 2 April 1999).
5. Wagner EH. Chronic disease management: what will it take to improve care for chronic illness? *Effective Clinical Practice* 1998; 1:2-4.
6. About chronic disease: definition, overall burden, and cost effectiveness of prevention. U.S. Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion. www.cdc.gov/nccdphp/about.htm (accessed 15 April 1999).

Mail

Fatal peyote ingestion associated with Mallory-Weiss lacerations

To the editors,

Although mescaline use is often viewed as posing a minimal health risk, we encountered a case demonstrating that ingestion can be fatal. Peyote cactus buttons *(Lophophora williamsii)* are brewed into a tea to release mescaline (3,4,5-trimethoxphenethylamine), a hallucinogenic alkaloid, and are used for Native American religious ceremonies.[1] The only fatality previously described with mescaline use was from trauma during a drug-induced delirium.[2] Botulism can be a consequence of peyote ingestion if the cactus buttons are stored in water.[3] We report a case of fatal mescaline intoxication associated with Mallory-Weiss esophageal lacerations.

Physicians treating Native Americans should consider the possibility of peyote use in cases of unexplained esophageal lacerations.

A 32-year-old Native American man with a history of alcoholism ingested peyote tea. After an uncertain period of time with unknown symptoms, he developed respiratory distress and suddenly collapsed. He was transported to a hospital and died after unsuccessful resuscitative efforts. Autopsy demonstrated 4 separate 1 cm lacerations at the gastroesophageal junction, 45 ml of gastric luminal blood, duodenal blood, and marked pulmonary hemoaspiration. His liver had marked fatty change consistent with chronic alcoholism. An antemortem blood specimen contained 0.48 mg/L of mescaline and a urine specimen 61 mg/L of mescaline when analyzed by gas chromatography/mass spectrometry. A trace amount of chlordiazepoxide was also found in a blood specimen. No other drugs of abuse or ethanol were detected. Vitreous fluid electrolyte, creatinine, urea nitrogen, and glucose concentrations were normal. The cause of death was certified as mescaline intoxication.

Mescaline is related to synthetic amphetamine derivatives used as street drugs.[1] Physiologically, mescaline can produce both increases and decreases in blood pressure and heart rate, respiratory depression, and vasodilation.[4] Mescaline is well known for its emetic effects.[4] Other substances that induce vomiting, such as ipecac, have caused Mallory-Weiss lacerations.[5] The Mallory-Weiss esophageal lacerations in this case were probably a consequence of mescaline-induced forceful vomiting. The mechanism of death was likely hemoaspiration, although an additional adverse pharmacodynamic effect of mescaline on the cardiovascular system cannot be excluded. Physicians treating Native Americans should consider the possibility of peyote use in cases of unexplained esophageal lacerations. The use of peyote for religious or recreational purposes is not without risk.

Kurt B Nolte, MD
Office of the Medical Investigator
University of New Mexico School of Medicine
Albuquerque, NM 87131-5091

Medical Examiner/Coroner Information Sharing Program
National Center for Environmental Health
Centers for Disease Control and Prevention
Atlanta, GA 30341

Ross E Zumwalt, MD
Office of the Medical Investigator
University of New Mexico School of Medicine
Albuquerque, NM 87131-5091

References

1. Baselt RC, Cravey RH. Mescaline. In: Baselt RC, Cravey RH, eds. *Disposition of toxic drugs and chemicals in man.* Fourth ed. Foster City, CA: Chemical Toxicology Institute, 1995:466-7.
2. Reynolds PC, Jindrich EJ. A mescaline associated fatality. *J Anal Tox* 1985; 9:183-4.
3. Hashimoto H, Clyde VJ, Parko KL. Botulism from peyote (letter). *N Engl J Med* 1998; 339:203-4.
4. Kapadia GJ, Fayez MBE. Peyote constituents: chemistry, biogenesis, and biological effects. *J Pharm Sci* 1970; 59:1699-1727.
5. Tandberg D, Liechty EJ, Fishbein D. Mallory-Weiss syndrome: an unusual complication of ipecac-induced emesis. *Ann Emerg Med* 1981; 10:521-3.

Original Research

Review of published criteria for evaluating health-related websites

Paul Kim
Thomas R Eng
Health Communication and Telehealth
Office of Disease Prevention and Health Promotion
U.S. Department of Health and Human Services
200 Independence Ave SW, Room 738G
Washington, DC 20201

Mary Jo Deering
Andrew Maxfield
National Institute for Occupational Safety and Health
Centers for Disease Control and Prevention
HHS Building
200 Independence Ave SW, Room 733G
Washington, DC 20201

Correspondence to:
Dr Eng
teng@osophs.dhhs.gov

Conflicts of interest:
None declared.

Abstract ● **Objective** To review published criteria for specifically evaluating health-related information on the World Wide Web and to identify areas of consensus in evaluation. ● **Design** Search of Web sites and peer-reviewed medical journals for explicit criteria for evaluating health-related information on the Web using Medline and Lexis-Nexis databases and the following Internet search engines: Yahoo!, Excite, Altavista, Webcrawler, HotBot, Infoseek, Magellan Internet Guide, and Lycos. Criteria were extracted and grouped into categories. ● **Results** Twenty-nine published rating tools and journal articles were identified that had explicit criteria for assessing health-related Web sites. Of the 165 criteria extracted from these tools and articles, 132 (80%) were grouped under 1 of 12 specific categories, and 33 (20%) were grouped as miscellaneous because they lacked specificity or were unique. The most frequently cited criteria were those dealing with the content, design, and aesthetics of a site; disclosure of authors, sponsors, or developers; currency of information (includes frequency of update, freshness, and maintenance of site); authority of source; ease of use; and accessibility and availability. ● **Conclusions** Many authors agree on the key criteria for evaluating health-related Web sites and efforts to develop consensus criteria may be helpful. The next step is to identify and assess a clear, simple set of consensus criteria that the general public can understand and use.

Introduction

The large volume of health information resources available on the Internet has great potential to improve health,[1-3] but it is increasingly difficult to discern which resources are accurate or appropriate for users.[3-8] Because of the potential for harm from misleading and inaccurate health information,[9-14] many organizations and individuals have published or implemented criteria for evaluating the appropriateness or quality of these resources.[15,16] Two published reviews of evaluation criteria for health-related Web sites did not present information on the range of criteria proposed by various authors and included rating tools that were not developed exclusively for health-related sites.[15-17] Our study reviews criteria currently proposed or used specifically to evaluate health-related Web sites.

Methods

Between September 1997 and May 1998, we conducted a search of the Web and of peer-reviewed medical journals for criteria for evaluating health-related information on the Web. We used the Medline and Lexis-Nexis databases and search engines including Yahoo!, Excite, Altavista, Webcrawler, HotBot, Infoseek, Magellan Internet Guide, and Lycos. Medline searches (using PubMed) used variations of the following: "quality," "Internet," "World Wide Web," "computer communication networks/standards," "quality control," and "medical informatics/standards." Searches with search engines and Lexis-Nexis used "quality," "health information," "health," and variations of "rating," "ranking," "evaluate," "award," *and* "assess." Investigating references and hyperlinks from initial results identified additional resources. We ended the sampling period when searches produced similar results and when previous search results became outdated.

Criteria

We included criteria if they were explicit, specifically used for evaluating health-related Web sites, and published in a peer-reviewed journal or publicly accessible Web site. We also considered peer-reviewed journals not indexed by Medline. We included resources framed as "guidelines" because there was little difference between them and other criteria and the intent of the authors was similar. When subcriteria provided details about main criteria, we included only the main criteria to prevent overrepresenting that author's perspective. Criteria were extracted and sorted into similar groups according to their wording and description. When a criterion seemed to combine several concepts and could fit into multiple groups, we considered the first mentioned concept.

To examine the reproducibility of the criteria groupings, 4 independent, naive coders assigned 40 randomly selected criteria to the 13 criteria groups. Overall, the coders' assignment of criteria agreed with us 76% of the time. The

agreement coefficient, indicating "percent agreement above chance," was 0.74.[18] (An extended methods section appears on the World Wide Web at www.bmj.com.)

Results

Twenty-nine rating tools and articles (24 Web sites and 5 journal articles) had explicit criteria for assessing health-related Web sites (Table 1). Of the 165 criteria identified, 132 (80%) were grouped under 12 specific categories (Table 2). Thirty-three (20%) criteria that lacked specificity or were unique were categorized as "miscellaneous." Frequently cited criteria included those dealing with the content, design, and aesthetics of a site and disclosure of authors, sponsors, or developers.

Discussion

Not surprisingly, "content" of the site, which includes concepts of information quality and accuracy, was the most commonly cited criterion group. Design and aesthetics of the site and ease of use were the second and sixth most frequently cited groups respectively, indicating that authors highly value good-quality application design and user interfaces. Disclosure of authors, sponsors, or developers was the third most frequently cited group, highlighting the need for users to be able to consider a site's content in the context of who created or financed the site. It was somewhat surprising that disclosure was not more commonly cited, given recent reports about misleading health information and fraud on the Internet.[9, 11, 12] Most rating tools discriminated between content and the fourth most common criterion group, currency of information (which includes the frequency of updates, freshness of data, and site maintenance), suggesting that currency of information is nearly as important as the information itself.

Table 1 *Rating tools and journal articles with explicit criteria for evaluation of health-related websites*

Source of rating tool or article	URL address*
AltiMed/PharmaLINKS	www.altimed.com/links/ratings.html
American Medical Association	www.ama-assn.org/med_link/med_link.htm
Biosites, Pacific Southwest Regional Medical Library	www.library.ucsf.edu/biosites/help/guidelines.html
British Healthcare Internet Association	www.bhia.org/public/reference/recommendations/medpubstandards.htm
Growth House	www.growthhouse.org/award.html
Health A to Z	www.healthatoz.com/aboutus.htm
Health Information Institute's Aesculapius Awards	www.hii.org/judging.htm
Health On the Net Foundation	www.hon.ch/HONcode/Conduct.html
Health Summit I Mtg/Mitretek Systems	www.mitretek.org/hiti/showcase/documents/criteria.html
Health Web	healthweb.org/wg/content/papers/guidelines.html
Healthfinder	www.healthfinder.gov/aboutus/selectionpolicy.htm
Larkin, M. Health information on-line. *FDA Consumer* 1996; 30:21-5.	www.fda.gov/fdac/features/596_info.html
McGill University Health Sciences and Osler Libraries, Canada	www.health.library.mcgill.ca/resource/criteria.htm
Medical Matrix	www.medmatrix.org/info/sitesurvey.html
Medsite Navigator, Guide to Digital Science and Medicine	www.medsitenavigator.com/mail/submit.html
Mental Health Net	www.cmhc.com/help/ratings.htm
Mountain and Plains Partnership	www.uchsc.edu/csa/areahec/home/mapp/8aWWW.html#public
Nutrition Navigator	navigator.tufts.edu/ratings.html
Organizing Medical Networked Information	omni.ac.uk/agec/evalguid.html
Physician's Choice	www.mdchoice.com/instruc.htm
Psych Central: Best of the Web in Mental Health	www.grohol.com/rateguid.htm
Reference 6	www.ama-assn.org/sci-pubs/journals/archive/jama/vol_277/no_15/ed7016x.htm
Reference 8	www.bmj.com/archive/7098ip2.htm
Reference 16	Not available online
Reference 19	Not available online
Sympatico's HealthyWay Health Links	www1.sympatico.ca/healthyway/GENERAL/info_2.html
The Six Senses Review	www.sixsenses.com/FAQ.html#rating
The Virtual Hospital	indy.radiology.uiowa.edu/Beyond/PeerReviews/01Introduction.html
The Wilton Library	w3.nai.net/~wla/eval.htm

*Because of the dynamic nature of the World Wide Web, some URLs may have changed. URLs prefixed with http://

Table 2 *Frequency of explicit criteria for evaluation of health-related web sites by criteria groups**

Criteria groups	Frequency (%)	(n=165)
Content of site (includes quality, reliability, accuracy, scope, depth)	30	(18)
Design and aesthetics (includes layout, interactivity, presentation, appeal, graphics, use of media)	22	(13)
Disclosure of authors, sponsors, developers (includes identification of purpose, nature of organization, sources of support, authorship, origin)	20	(12)
Currency of information (includes frequency of update, freshness of data, maintenance of site)	14	(8)
Authority of source (includes reputation of source, credibility, trustworthiness)	11	(7)
Ease of use (includes usability, navigability, functionality)	9	(5)
Accessibility and availability (includes ease of access, fee for access, stability)	9	(5)
Links (includes quality of links, links to other sources)	5	(3)
Attribution and documentation (includes presentation of clear references, balanced evidence)	5	(3)
Intended audience (includes nature of intended users, appropriateness for intended users)	3	(2)
Contact addresses or feedback mechanism (includes availability of contact information, contact address)	2	(1)
User support (includes availability of support and documentation for users)	2	(1)
Miscellaneous (includes criterion that lacked specificity or were unique)	33	(20)

Percentage total does not equal 100 due to rounding-off.

*Of 5 authors who assigned weights or priorities to their proposed criteria, 4 cited content and 1 cited peer review (categorized as miscellaneous) as the most important criterion.

Criteria related to confidentiality and privacy of information were only cited by one author, despite widespread interest in this issue.[20] Some health-related Web sites are already collecting personal health information to "tailor" content, and as sites begin to integrate health care services and information, confidentiality and privacy safeguards will become increasingly important.[20-22]

The limitations of our review include the subjective variables around the scope of the criteria categories used. Testing of the category groupings, however, showed that they were reproducible by others. It is also possible that some authors used the same terms for criteria to describe different concepts. Because subcriteria were not included, some concepts may not have been represented. The inherent limitations of search engines and the dynamic nature of the Web also prevented us from locating all existing published criteria.[23] Nevertheless, our review located more sources of criteria specifically for health-related sites than did previous reviews.[15, 17]

Key messages

- Many organizations and individuals have published criteria to evaluate health-related information on the World Wide Web
- A search of the literature and the Web found that the most frequently cited criteria were those dealing with the content, design, and aesthetics of a site; the disclosure of authors, sponsors, or developers; the currency of information; the authority of the source; and ease of use
- Criteria related to confidentiality and privacy were only cited by one author
- A consensus on the critical criteria for evaluating Web-based health information seems to be emerging
- Many authors agree on key criteria for evaluating health-related Web sites, and efforts to develop a set of key criteria may be helpful

Conclusion

Given the evolving state of the Internet, it may be difficult or even inappropriate to develop a static tool or system for assessing health-related Web sites. Our results suggest that many authors agree on key criteria and that efforts to develop consensus criteria may be helpful.[6, 16, 24-26] The next step is to identify and assess a clear, simple set of consensus criteria that the public can understand and use. Tools that integrate the criteria need to be developed and validated, and their ultimate impact and effectiveness in assisting the public with health-related decisions should be monitored to ensure that they remain useful.

We thank Farrokh Alemi and Anne Restino for their assistance and advice on this study.

Contributors: PK participated in data collection, analysis, and interpretation, and in writing the paper. TRE formulated the study design, developed the core ideas, and participated in data analysis and interpretation and in writing the paper. MJD participated in designing the study, interpreting the data, and editing the paper. AM participated in data analysis and interpretation and in editing the paper. PK and TRE will act as guarantors for the paper.

Funding: Internal funds of the U.S. Department of Health and Human Services. The views expressed in this paper are solely those of the authors and do not necessarily reflect those of the U.S. Department of Health and Human Services.

This paper originally appeared in the *BMJ* 1999; 318:647-9.

References

1. Government Accounting Office. *Consumer health informatics: emerging issues.* Publication of the Government Accounting Office/Accounting and Information Management Division—96-86, July 1996.
2. Robinson TN, Patrick K, Eng TR, Gustafson D for the Science Panel on Interactive Communication and Health. An evidence-based approach to interactive health communication: a challenge to medicine in the information age. *JAMA* 1998; 280:1264-9.
3. Eng TR, Maxfield A, Patrick K, Deering MJ, Ratzan S, Gustafson D. Access to health information and support: a public highway or a private road? *JAMA* 1998; 280:1371-5.
4. Coiera E. The internet's challenge to health care provision. *BMJ* 1996; 312:3-4.
5. The web of information inequality [editorial]. *Lancet* 1997; 349:1781.
6. Silberg WM, Lundberg GD, Musacchio RA. Assessing, controlling, and assuring the quality of medical information on the internet. Caveant lector et viewor—let the reader and buyer beware. *JAMA* 1997; 277:1244-5.
7. Sonnenberg FA. Health information on the internet: opportunities and pitfalls [editorial]. *Arch Intern Med* 1997; 157:151-2.
8. Wyatt JC. Commentary: measuring quality and impact of the world wide web. *BMJ* 1997; 314:1879-81.
9. Federal Trade Commission. North American Health Claim Surf Day targets internet ads: hundreds of e-mail messages sent. Press release, Nov. 5, 1997. (www.ftc.gov/opa/9711/hlthsurf.htm [May 12, 1998].)
10. Impicciatore P, Pandolfini C, Casella N, Bonati M. Reliability of health information for the public on the world wide web: systematic survey of advice on managing fever in children at home. *BMJ* 1997; 314:1875-9.
11. Food and Drug Administration. FDA warns consumers on dangerous products promoted on the internet. FDA Talk Paper T97-26, June 17, 1997.
12. Bower H. Internet sees growth of unverified health claims. *BMJ* 1996; 313:497.
13. Micke MM. The case of hallucinogenic plants and the internet. *J Sch Health* 1996; 66:277-80.
14. Weisbord SD, Soule JB, Kimmel PL. Poison on line: acute renal failure caused by oil of wormwood purchased through the internet. *N Engl J Med* 1997; 337:825-7.
15. Jadad AR, Gagliardi A. Rating health information on the internet: navigating to knowledge or to Babel? *JAMA* 1998; 279:611-4.
16. Pealer LN, Dorman SM. Evaluating health-related web sites. *J Sch Health* 1997; 67:232-5.
17. Murray PJ, Rizzolo MA. Web site reviews and evaluations. *Nurs Stand Online* 1997 Jul 30; 11(45). (www.nursing-standard.co.uk/vol11-45/ol-art.htm [January 29, 1998].)
18. Krippendorf K. *Content analysis: an introduction to its methodology.* Beverly Hills, CA: Sage, 1980.
19. Kotecki JE, Siegel DE. Electronic notes: use of a criticial thinking/questioning approach to evaluate WWW information. *Am J Health Behav* 1998; 22:75-6.
20. Bowen JW, Klimczak JC, Ruiz M, Barnes M. *Design of access control methods for protecting the confidentiality of patient information in networked systems.* Proceedings of the American Medical Informatics Association annual fall symposium. American Medical Informatics Association, 1997:46-50.
21. National Research Council, Computer Science and Telecommunications Board (US). *For the record: protecting electronic health information.* Washington: National Academy Press, 1997.
22. Patrick K, Robinson TN, Alemi F, Eng TR for the Science Panel on Interactive Communication and Health. Policy issues relevant to the evaluation of interactive health communication applications. *Am J Prev Med* 1999; 16:35-42.
23. Lawrence S, Giles CL. Searching the world wide web. *Science* 1998; 280:98-100.
24. British Healthcare Internet Association. Quality standards for medical publishing on the web. (www.bhia.org/public/reference/recommendations/medpubstandards.htm [May 26, 1998]).
25. Health On the Net Foundation. HON code of conduct for medical and health web sites. (www.hon.ch/HONcode/Conduct.html [January 27, 1998]).
26. Health Information Technology Institute, Mitretek Systems. Criteria for assessing the quality of health information on the internet. (www.mitretek.org/hiti/showcase/index.html [January 27, 1998]).

COMMENTARY

How patients use the web for second opinions

Kevin Patrick
Student Health Services
San Diego State University, San Diego, CA 92182-4701
kpatrick@shsin.sdsu.edu

Do I need a prostate-specific antigen test? Should I change my allergy medication? Do I really need surgery for this lump in my breast? Where can I find the best specialist care for my child's illness? Our patients and their families have many important questions. Traditionally, one's personal physician has been the professional source first turned to for answers. The time-honored role of the physician is as a counselor as much as a healer. Information provided by a trusted professional can override uncertainty and confusion and bring peace of mind, hope, and even healing.

Times change, however, and with them the means to answer health and medical related questions. Witness the Internet, increasingly available in homes, workplaces, libraries and schools. A recent Harris poll found that 60 million American adults, 68% of those who use the Internet, have used the World Wide Web to find health information. Who among the practicing medical profession can't describe a recent instance in which a patient begins a question with: "I was reading on the web the other night and…"? Sometimes, this can be a pleasant experience in which both doctor and patient share in mutual edification. On the other hand, sometimes the information the patient gleaned from the Web might vary from the clinician's own knowledge and experience. Time permitting, this presents an excellent opportunity for patient

(or doctor) education. Unfortunately, time doesn't always permit, and in some cases, the tone of the clinical encounter goes rapidly downhill leaving both patient and provider dissatisfied.

So how does one respond to the increasing use of the Web for "second opinions?" One way is to become familiar with the criteria by which purveyors of Web-based health information are being judged. This issue of *WJM* presents a review of these criteria (see p.329). The authors searched for all on-line tools, published reports, and recommendations about how to judge the quality of information on health-related Web sites. What was surprising was that only one paper explicitly mentioned assurances of confidentiality and privacy as a criterion worth considering. Privacy and confidentiality of health information is an ever-present concern at both the national[1] and regional[2] levels. As the authors and others[3] have pointed out, this may be one of the most important issues as Web-related health information and clinical health information systems increasingly merge in the future.

Familiarity with the criteria outlined in this paper can be valuable. While most health care providers won't have the time to explore even a fraction of the health information on the Web, discussing these criteria with a patient can productively reframe the often uncomfortable "But the web said this" situation. Who said it? What sources did they site? Did they disclose a financial interest in their point of view? How current was the information? Did they convey that this was an area about which reasonable differences of opinion exist? Evidence-based approaches to assuring the quality of Web and other interactive health communication[4] should be invoked when and where possible.[5] As our patients increasingly turn to the web for information and support, helping them learn the right questions to ask may become one of our most important roles.

References

1. Health privacy and confidentiality recommendations, National Committee on Vital and Health Statistics, June 25, 1997. (http://aspe.hhs.gov/ncvhs/privrecs.htm).
2. Promoting Health And Protecting Privacy, California Healthcare Foundation and Consumers Union, January 1999 (www.chcf.org).
3. Patrick K, Robinson TN, Alemi F, Eng TR, for the Science Panel on Interactive Communication and Health. Policy issues relevant to the evaluation of interactive health communication applications. *Am J Prev Med* 1999; 16: 35-42.
4. Robinson TN, Patrick K, Eng TR, Gustafson D, for the Science Panel on Interactive Communication and Health. An evidence-based approach to interactive health communication: a challenge to medicine in the Information Age. *JAMA* 1998; 280:1264-9.
5. Science Panel on Interactive Communication and Health. *Wired for Health and Well-Being: the Emergence of Interactive Health Communication*. Eng TR, Gustafson DH, editors. Washington, DC: U.S. Department of Health and Human Services, Government Printing Office, April 1999.

Netphiles

Although much associated with modern technology and today's breakthroughs, the internet has not ignored the past, as witnessed by an online exhibition of the history of medicine. The Web site, **http://www.nlm.nih.gov/exhibition/exhibition.html**, comes from the prestigious U.S. National Library of Medicine. The site contains some fascinating material—for example, a section on the history of the cesarean. There are some superb illustrations and, at the bottom of the page, there are links to other services in this substantial site such as Medline.

The internet is a superb repository of information about rare and unusual diseases, but the problem is often tracking down the relevant data. There are some highly rated search engines around, but a good place to start is **rarediseases.info.nih.gov/ord/site@index.html**, is the site index of the U.S. based Office of Rare Diseases. From here, readers can rapidly assess the relevance of the site to their information requirements. The site also provides links, each with a brief description of the site, to an array of high quality Web resources where more specific information can be found on a rare disorder.

Similarly, the Web is an ideal medium for publishing databases, and there are plenty available, but finding them can be a problem. An excellent guide can be found at **www.shef.ac.uk/~scharr/ir/trawling.html**. This first class collection will be of interest to a wide variety of health professionals. Each database merits a concise description with, of course, hypertext links that take you directly to the reviewed site. Usefully, all the sites chosen are free to access.

If you want a good all-round resource for pediatric surgery then look no further than **home.coqui.net/titolugo/index.htm**. It originates from Puerto Rico and is bristling with useful and relevant information, including a journal and a handbook as well as a links page. There is also information about relevant meetings and bodies such as the associated pædiatric surgical department. All this and more is neatly packaged into a colorful and well designed Web site.

If you use a personal computer regularly or even infrequently then you should be interested in the contents of **www.pc.ibm.com/us/healthycomputing/index.html**. This site is produced by IBM and is a detailed review of how to look after your own or your staff's health and working environment while using a computer. It is an interesting and educational read, and all computer users would probably benefit from spending time absorbing some of the facts and data highlighted here.

The Johns Hopkins Infectious Disease Web site at **hopkins@id.edu** has plenty to offer both casual surfers and serious researchers. The home page provides a useful launch pad to explore the various components of the site, and the in-house search engine should help to pinpoint any specific information that you require. Among the more usual material that you would expect to find, the tables of facts and figures in "Bartlett's Top 10" (**hopkins@id.edu/idfun/topten/index_topten.html**) provide some fascinating insights into the world of infectious diseases.

—Harry Brown, Leeds, DrHarry@dial.pipex.com

We welcome suggestions for Web sites to be included in future Netphiles

Med.Pix

A rash on the feet and buttocks

Richard P Usatine
UCLA
200 UCLA Medical Plaza, Suite 220
Los Angeles, CA 90095-1628

Correspondence to:
rusatine@ucla.edu

QUESTION: An 18-month-old boy was brought to the doctor's office by his mom for an itchy rash on his feet and buttocks. The physician examined the child and made the presumptive diagnosis of ringworm (*Tinea corporis*). Topical clotrimazole cream was prescribed. After 2 weeks of continued symptoms, the distraught mom brought the child to an urgent care center. The child had been unable to sleep at night due to the intense itching. He was losing weight secondary to his poor appetite. The physician learned that the family had returned from a trip to the Caribbean prior to the first visit to the physician. The child had played on beaches that were frequented by local dogs. The physical exam revealed the lesions seen in Figures 1 and 2. What is the real diagnosis?

Figure 1

Figure 2

Figure 3

ANSWER: On the second visit, the physician recognized the serpiginous burrows of cutaneous larva migrans (creeping eruption). Cutaneous larva migrans is caused by cat or dog hookworm larvae. These larvae penetrate the unbroken skin of humans and migrate through the skin, looking for the intestines. Never making it that far, the larvae stay concealed ahead of the raised erythematous linear tracks in the skin. The adult hookworm lives in the intestines of dogs and cats and the ova are excreted in the feces. In this case, the child sat in the contaminated soil or sand of a Caribbean beach.

How could cutaneous larva migrans be mistaken for ringworm? Ringworm is caused by dermatophyte fungus. A typical case is seen in Figure 3. There is no worm in ringworm. Ringworm has an annular appearance with central clearing. There is redness and scaling on the perimeter of this well-demarcated lesion. Although this annular lesion can appear to be created by a worm, its appearance is due to the centrifugal growth of the fungus. Both conditions have well-demarcated borders and can have ringlike geometry. Both lesions may be related to exposure to infected cats or dogs. Note that the 5-year-old girl in Figure 3 has a cat on her shirt. There was a cat in the home with some patches of hair loss. This infection could be due to *Microsporum canis,* a zoophilic dermatophyte that primarily infects animals but occasionally infects humans.[1] A skin scraping was done, and branching hyphae were identified with light microscopy.

Diagnosis and treatment of cutaneous larva migrans

The diagnosis is based on the typical appearance of the serpiginous burrows, especially on the feet or buttocks. A positive history of sitting on sand or soil in a tropical region supports this diagnosis. There may be eosinophilia in the blood, but this is neither necessary nor sufficient to make the diagnosis. The treatment of choice is topical thiabendazole applied 2 to 3 times per day for 5 days.[2,3] If topical treatment fails, oral albendazole or oral ivermectin are preferred due to the high frequency of adverse effects with oral thiabendazole.[2,3]

Diagnosis and treatment of ringworm

A skin scraping treated with potassium hydroxide (KOH) and analyzed with a microscope can be helpful when classic hyphae are found on the slide. Fungal cultures provide the most definitive evidence of fungal infection along with the identity of the fungus. Small infections like the one seen in Figure 3 usually respond well to over-the-counter topical antifungals (miconazole, clotrimazole). Large areas of involvement may require oral antifungal treatment.

Outcomes

Both children responded to topical therapies, and the conditions healed with no scarring.

References

1. Radentz WH. Fungal skin infections associated with animal contact. *Am Fam Physician* 1991; 43:1253-1256.
2. Habif T. *Clinical dermatology: a color guide to diagnosis and therapy.* Third Edition. Mosby, 1996.
3. Davies HD, Sakuls P, Keystone JS. Creeping eruption. A review of clinical presentation and management of 60 cases presenting to a tropical disease unit. *Arch Dermatol* 1993; 129:588-591.

How to submit your medical images for publication in Med.Pix

Do you have images (slides, photos, etc.) of compelling visual cases in clinical medicine?
If other primary care providers would find them interesting, we would like to publish them, along with a brief description of the clinical presentation and a question for the readers. The answer should provide an explanation of the clinical case along with information on differential diagnosis and treatment. The treatment section should suggest an evidence-based approach and be supported by current references. Multiple images may be submitted and interesting connections between these images may be highlighted.

High quality slides, illustrations, and photographic prints may be mailed to:
Richard Usatine, MD; Section Editor, Med.Pix; 200 UCLA Medical Plaza, Suite 220 Los Angeles, CA 90095-1628; Fax 310-206-0181.

Written descriptions and electronic images may be submitted to: rusatine@mednet.ucla.edu.

Note: If the patient's identity is recognizable, a signed permission form should accompany the submission materials.

Research Digest

A brief smoking cessation intervention for adults in hospital is cost-effective

Meenan RT, Stevens VJ, Hornbrook MC, et al. *Med Care* 1998; 36:670-8.

Correspondence to:
Dr Meenan
Kaiser Permanente Center for Health Research
3800 N Kaiser Center Drive
Portland, OR
97227-1098

Funding: National Cancer Institute.

Question
Is an in-hospital smoking cessation program for a general population of adult patients cost-effective?

Design
Cost-effectiveness analysis from the perspective of the implementing hospital, using data from a controlled trial with follow-up at 12 months.

Setting
Two 200-bed hospitals managed by Kaiser Permanente Northwest health maintenance organization in Oregon and Washington.

Patients
A total of 1119 patients ≥18 years of age (mean age 44 years, 62% women)[1] who reported smoking regularly in the previous 3 months. Patients with a hospital stay <36 hours as well as those who were postpartum, admitted for substance abuse, or receiving hospice care were excluded.

Intervention
Altogether, 453 patients were allocated to the intervention and were offered 20 minutes of bedside counseling with an experienced counselor, a 12-minute video, self-help materials, and 1 to 2 follow-up telephone calls after discharge.[1] A total of 666 patients received usual care.[1]

Main outcome and cost measures
Quit rates (self-reported consecutive abstinence from all tobacco use); incremental quit rate (number of patients who quit in the intervention group minus the number who quit in the usual care group); cost per incremental quit (incremental costs per smoker divided by incremental quit rate); and discounted life-years saved (DLYS). Life-years saved were estimated from published data on smoking-related changes in life expectancy. Total intervention costs included costs to identify newly admitted smokers, solicit cooperation, deliver bedside counseling, and follow up after discharge. All costs were reported in 1994 dollars.

Smoking cessation intervention vs usual care at 12 months

Outcome	Intervention	Usual care	Increase in relative risk (95% CI)*	Number needed to treat (95% CI)*
Abstinence	13.5%	9.2%	47% (5.3 to 105)	23 (12 to 174)

*Increase in relative risk, number needed to treat, and confidence intervals calculated from data in article.

Main results
An intention-to-treat analysis was used. At 12 months, patients who had received the smoking cessation intervention had higher quit rates than patients who had received usual care (P=0.02) (see Table). The cost per incremental quit was $3,697. At a 5% discount rate and an incremental quit rate of 4.3%, the cost per DLYS was $3,680, which compares favorably with other well-accepted health care interventions. Sensitivity analysis found incremental costs per incremental DLYS ranging from $909 to $53,347 when the quit rate was varied from 8.0% to 0.6% and the discount rate was varied from 2% to 8%.

Conclusion
An in-hospital smoking cessation intervention delivered to a general population of adult patients was cost-effective.

COMMENTARY
Patricia W Stone, Harvard University, Boston, MA

Previous research has found that nurse-managed smoking cessation programs for patients in the hospital with myocardial infarction are cost-effective.[2] The analysis by Meenan et al supports and extends these results. The lower cost-effectiveness ratios associated with inpatient counseling programs compared with outpatient educational programs[3] support the notion of a "teachable moment" when smokers are more likely to respond to a cessation message.

The original trial on which the economic analysis was based was not randomized. To avoid contamination, the hospital in which patients received the intervention was alternated each month.[1]

The original study took place in 2 hospitals that had smoke-free policies requiring at least temporary cessation by patients who smoked. The results may not therefore be generalizable.

Only 52% of patients provided samples for biochemical confirmation of abstinence.* Because of this low rate, it is possible that participants misreported their smoking status. The authors, however, used sensitivity analyses to estimate cost-effectiveness even if the incremental quit rate fell from 4.3% to 0.6%.

By combining published data on smoking-related changes in life expectancy with overall life expectancy, the analysts could more accurately predict the long-term effects of smoking cessation for individuals with differing smoking habits. The long-term outcomes were discounted, which assumes that people place greater value on something they have today rather than on something they will have in the future. The authors were able to investigate the impact of discounting using sensitivity analyses.

*Data provided by authors.

1 Stevens VJ, Glasgow RE, Hollis JF, et al. A smoking-cessation intervention for hospital patients. *Med Care* 1993; 31:65-72.
2 Krumholz HM, Cohen BJ, Tsevat J, et al. Cost-effectiveness of a smoking cessation program after myocardial infarction. *J Am Coll Cardiol* 1993; 22:1697-702.
3 Salkeld G, Phongsavan P, Oldenburg B, et al. The cost-effectiveness of a cardiovascular risk reduction program in general practice. *Health Policy* 1997; 41:105-19.

This article was originally published in *Evidence-Based Nursing* 1999; 2:58.

Learning how to live with a child with ADHD is a long process

Question
How do families with children who have attention deficit hyperactivity disorder (ADHD) manage the persistent difficulties caused by their children's symptoms?

Design
Grounded theory.

Setting
United States.

Participants
A total of 15 families (14 white) with ≥1 child with ADHD between the ages of 6 and 18 years. The ADHD child and ≥1 parent had to be willing to participate. Fifteen mothers, 10 fathers, 20 children with ADHD (mean age 11 years, 16 boys), and 14 siblings without ADHD (mean age 11 years, 8 boys) were interviewed. Five families had a single mother, 7 had both biological parents living at home, and 3 had a biological mother and a stepfather.

Methods
Altogether, 109 individual and family open-ended interviews, each lasting 30 to 90 minutes, were done in the home. Each person was asked to describe what it was like to live with ADHD or with a family member with ADHD and how their family functioned. Second individual and family interviews were done 8 to 12 weeks later.

Main findings
Outlasting disruption was the core variable. Family life was described as chaotic, conflictual, and exhausting. Disruptive behaviors were aggression, out-of-control hyperactivity, emotional and social immaturity, academic underachievement and learning problems, family conflicts, negative peer interactions, and isolation and rejection from the extended family. Parents regained control over their lives *(process of reinvestment)* using a 3-step model *(making sense, recasting biography,* and *relinquishing the good ending).*

Making sense had 4 categories. *Sinking in* dealt with being able to admit that a problem existed. *Believing* dealt with coming to terms with the child's identified problem and working toward normal functioning. *Wearing out* was a cyclical process of getting stuck, giving up, recharging, burning out, and getting stuck again. *Transferring responsibility* included relinquishing the idea that normal functioning was possible.

Recasting biography involved parents' examining their lives and developing new directions. Its categories were *remembering* their own childhood difficulties; *grieving* for past and current situations and the child's inability to become a strong and self-confident adult; *individuating,* which occurred when the mother realized that she had to "separate" from the child (often a son); and *restoring self,* in which parents put energies back into themselves and felt comfortable with who they were.

Relinquishing the good ending was the final process. It involved letting go of the belief that a child with ADHD was just like everyone else and moving beyond grief. The categories were *deintegrating stigma* by examining their own beliefs about ADHD, *gaining perspective* by changing old beliefs and fostering an emotional acknowledgment of the disorder, and *letting go of the anticipated normal child.* Once these processes were complete, parents were able to come to terms with the child's disability and engage in reinvestment in the "real" children, family, other children, marriage, and themselves.

Conclusion
Parenting a child with ADHD was a long and arduous process. Parents outlasted the disruption by making sense of the disorder, recasting biography, and relinquishing the good ending.

Kendall J. *Qual Health Res* 1998; 8:839-57.

Correspondence to:
Dr Kendall
Oregon Health Sciences University
School of Nursing
3181 SW Sam Jackson Road
Portland, OR 97201-3098

Funding: National Institute of Child Health and Human Development.

COMMENTARY

Steven Pryjmachuk, University of Manchester, Manchester UK

ADHD, a disorder involving inattentiveness, overactivity, and impulsivity, has been the subject of recent debate in child and adolescent mental health. Much of the debate has centered on establishing diagnostic criteria and on specific interventions; Kendall's study, in contrast, centers on the experiences of those who are part of a family that has a child with ADHD.

Although Kendall identifies a specific process and constituent subprocesses in the families studied, this is not the main strength of the study. Its main strength lies in the way in which it persuasively reminds the reader that the real-life experiences of those living with a specific mental health problem are equally effective in informing practice as are more formal sources such as textbooks. As Kendall herself points out, all too often the focus of any intervention with families similar to those described in the study is on training family members to be better caregivers or parents. Issues important to the families themselves, such as offering physical or emotional support, respite, or family-centered mental health services, are rarely given the attention they deserve.

Because the study gives us insight into the experiences of only a few families with a child with ADHD, the identification of specific processes is only useful if it is set to inform rather than prescribe. Moreover, as with any research, the study raises more questions than answers:

- Are the predominantly white, "high-functioning and well-educated" families included in the study typical of other families with children with ADHD?
- Are these families different from other families caring for a family member with special needs?
- Are similar processes evident in families that appear to be comparatively stress-free?
- What about families who do not outlast disruption?

This article was originally published in *Evidence-Based Nursing* 1999; 2:60.

Women develop multiple coping strategies to deal with menopausal transitions

Kittell LA, Kernoff Mansfield P, Voda AM.
Qual Health Res 1998; 8:618-33

Correspondence to:
Dr Kittell
137 Laurel Run
Portage, PA 15946
ajlak@csrlink.net

Funding: None.

Question

What are women's experiences of menopausal transitions, and how do they interpret and respond to the changes they experience?

Design

Grounded theory.

Setting

United States.

Patients

A total of 61 women who were experiencing menopausal transitions (changes in menstrual bleeding, hot flashes, and changes in feelings and emotions). The age range was 41 to 54 years. Most were white, middle-class, college-educated, and employed outside the home.

Methods

Women were interviewed by telephone (23 to 110 minutes for each interview, with most lasting from 40 to 45 minutes) and asked to describe the changes that they were experiencing, how they felt about the changes, and ways in which the changes were affecting their lives. Changes could be related to bleeding, hot flashes, feelings and emotions, sleep, appearance, energy level, weight, appetite, digestion, sexual feelings, or other areas. Data were analyzed, processes were identified, and a theory was developed.

Main findings

The basic core variable (social process) was described as *keeping up appearances.* Appearance encompassed all aspects of presentation of the self and perceptions of being a certain type of person. Women attempted to keep up appearances by *concealing changes* and by maintaining a sense of *control* in relation to physical and emotional changes. Women hid changes by keeping silent, keeping to themselves, detaching themselves, masking feelings or behaviors, avoiding discussions, diverting inquiries and ignoring, minimizing, or dismissing the effects of changes.

The unpredictability of the changes left women feeling as though they had no control over what was happening to them. They wanted control to avoid embarrassment and to be able to function with minimal disruption. Control was maintained through management strategies (increased self-monitoring and self-care, monitoring the environment and interactions with others, and making adjustments).

Women felt vigilant and anxious in situations that could potentially disclose their menopausal status and confident and secure when the threat of disclosure was absent. Women sought help or felt frustrated in situations of potential social exposure and felt silent and detached when the threat of exposure was absent.

Women's feelings about, and responses to, changes varied over time and according to the characteristics of the change. If they felt that the changes were normal and not disruptive, they felt secure and undisturbed. If they felt that the changes were unexplained or disruptive, they became vigilant and used strategies to find out what was happening and how to minimize the disruption. In cases in which they had no control and a high threat of social disclosure, women sought professional help.

Conclusions

When women experienced menopausal transitions, they sought to regain control of the physical and emotional changes to keep up appearances.

COMMENTARY

Debbie Kralik, Flinders University of South Australia, 36 Beeston Way, West Lakes, South Australia, Australia 5021

The study presented by Kittell et al provides an intimate description of the needs and concerns of women experiencing menopausal transitions and shows the individuality of the menopausal experience. Research that focuses on the feelings, behaviors, and daily challenges of women who are experiencing changes in their menstrual cycle has not previously been published.

Data were generated by a single telephone call to each participant, and the interviews were guided by a prepared interview schedule. The interview might not have provided the participants with an adequate opportunity to reflect and articulate the most important aspects of living through menopausal change. The validity of the process of analysis might have been enhanced if the women had been invited to review the findings. However, illustration of the women's experiences using their words verbatim has provided an understanding of how the researchers arrived at their findings.

Two key concepts emerged from the data: *concealment* and *control.* During menopausal transitions, women described a desire to conceal the changes they were experiencing from others and to maintain a sense of control over the social and functional aspects of their lives. From these concepts the researchers developed the core variable of *keeping up appearances.* The term "appearance" encompassed all aspects of the presentation of self.

This study shows how unpredictable life during menopausal transition can be, and its findings should be made widely available to women, who often seek medical intervention only when they can no longer tolerate or control their symptoms. Johnson's extensive previous research has shown that having accurate expectations reduces distress.[1]

Through this study, the reader is sensitized to the experiences of women living through menopausal transitions and, as such, the findings are not only important to nurses but also to the wider community.

[1] Johnson JE, Fielder V, Jones L, et al. *Self-regulation theory: applying theory to your practice.* Pittsburgh, PA: Oncology Nursing Press, 1997.

This article was originally published in *Evidence-Based Nursing* 1999; 2:62.

Best Practice

EVIDENCE-BASED CASE REVIEW

Heart failure: Part II.

Michael S Wilkes
General Internal Medicine and Health Services Research

Holly Middlekauff
Division of Cardiology

Jerome R Hoffman
Emergency Medicine Center
University of California
Los Angeles, CA

Correspondence to:
Dr Wilkes
mwilkes@ucla.edu

Conflicts of Interest:
None declared.

Recap: Mr. G., a 60-year-old, previously healthy retiree is now 3 weeks status post an uncomplicated MI and has just been readmitted to the hospital with an EF of 35%.

Sudden death accounts for approximately 50% of mortality in patients with heart failure.[1] Most result from a lethal arrhythmia. Routine monitoring of the EKG has not been shown to reduce mortality in otherwise asymptomatic persons with heart failure. Type I anti-arrhythmic drugs have no place in the management of patients like Mr. G., because their proarrhythmic effects increase as the EF falls. Despite research showing the benefit of ACE inhibitors in treating heart failure, up to 60% of patients are not given ACE inhibitors, and many patients who are prescribed them are given lower doses than recommended (recommended doses are enalapril, 10 mg BID; lisinopril, 10 mg QD; captopril, 50-100 mg BID).[2-9]

If Mr. G. is on an ACE inhibitor for heart failure, can he also be on aspirin?

When heart failure results from CAD, it makes sense to use both ASA and ACE inhibitors. This poses a problem, however, in that a major clinical effect of ACE inhibitors comes from stimulating prostaglandin synthesis, while aspirin inhibits prostaglandin synthesis. A double-blind cross-over study done to evaluate the effect of enalapril with and without aspirin found that enalapril was more effective at reducing systemic vascular resistance when given without aspirin.[10, 11] Nevertheless, given the benefits of aspirin, and pending more data, it is reasonable to conclude, for the time being at least, that the benefits of aspirin outweigh its risks in patients with coronary artery disease who are on ACE inhibitors. Another recent study suggests that because of a similar mechanism (inhibition of renal prostaglandins), nonsteroidal anti-inflammatory drugs (NSAIDs) limit the response to diuretics. It seems prudent to restrict NSAIDs when possible in patients with heart failure and to monitor carefully renal function and volume status of patients.[12]

Is there still a role for supplemental oxygen in CHF?

Studies have suggested that supplemental oxygen decreases cardiac output and increases systemic vascular resistance in patients with heart failure. This effect appears to be dose-dependent, so physicians should probably choose the lowest concentration of supplemental oxygen necessary.[13] Continuous positive airway pressure (CPAP), delivered by a tight-fitting face mask, can improve oxygenation, decrease respiratory work, and decrease ventricular afterload. The nasal equivalent of CPAP, called BiPAP (Bilevel Positive Airway Pressure), is generally more acceptable to patients and appears to be at least as effective in patients with CHF as well. The benefit may be greatest in patients with high pulmonary capillary wedge pressure (PCWP). It is especially useful to consider one of these modalities during an episode of acute pulmonary edema, but one must be willing to stop if it leads to deterioration.[14-16]

What is the role of diuretics in heart failure?

For decades diuretics, given by intravenous bolus, continuous IV drip, or orally, have represented the mainstay of therapy for heart failure patients. Oral therapy is generally safest, while a continuous IV drip may be the least safe method of administration.[17] When choosing a diuretic, the cost, site and mechanism of action, effect on electrolytes, dosage, half life, and time of onset should all be considered. The potassium-sparing diuretics have the advantage of not wasting potassium, but they are relatively weak diuretics. As heart failure worsens, it may be necessary to combine diuretics, and there is a benefit from combining diuretics that work at different sites. Despite their benefits in controlling symptoms of congestion (pulmonary and peripheral), diuretics are associated with a relatively high incidence of adverse reactions; for this reason physicians may choose other treatments. A prospective study evaluated the strategy for discontinuation of diuretic therapy and found that older patients were less able to be weaned. In one study of withdrawal from diuretic therapy, 4 patients out of 33 studied experienced sudden death.[13] It is wise to monitor patients on diuretics closely, and to be cautious when weaning patients from diuretics.

Is there a role for beta blockers in managing heart failure?

Although beta blockers have long been considered contraindicated in heart failure, there is now credible evidence that they have an important role, particularly in people with mild to moderate chronic failure.[18] Several randomized controlled trials suggest the benefits of adding a beta blocker to diuretics and ACE inhibitors in the setting of chronic heart failure.[19-21] This benefit is presumably achieved by reducing the sympathetic activity[22] and results in a delay in the progression of disease. Contraindications to beta blockers include bronchospastic disease, severe bradycardia, and possibly diabetes. Several studies, all manufacturer-supported, suggest that carvedilol, a nonselective beta antagonist with alpha blocker and antioxidant effects, appears to be effective[23, 24] (Other

long-acting beta blockers may be equally effective.) Of note, many beta blocker trials were biased in favor of beta blockers, because they included a "run-in period" during which all patients received beta blockers. After this initial period, patients who deteriorated or died on the beta blockers were excluded from the studies, and their bad outcomes were omitted from the study results. Furthermore, the remaining patients who were then randomized either had continuation or discontinuation of beta blockers, so that the studies were really comparing beta treatment with beta blocker withdrawal, which is well known to be deleterious in a substantial number of patients. The CIBIS II trial,[18] however, also found important benefit with beta blockers in an RCT that did not include a run-in period. This manufacturer-supported trial suggests a protective effect in chronic heart failure. Seventy-four patients with mild to moderate heart failure would have to be treated with ACE inhibitors for 1 year to prevent 1 death. In contrast, 29 patients would need to be treated with an ACE inhibitor plus beta blocker to prevent 1 death.[25] If beta blockers are to be used, they should be started only in patients with stable, compensated heart failure. Initial doses should be low, with slow upward titration as blood pressure is closely monitored. Benefits are to be expected only after the first month or two. The use of beta blockers may be an area where the primary care provider can find benefit from consulting a cardiologist.

What is the role of nitrates?

The clinical role of nitrates in the chronic care of chronic congestive heart failure has decreased, as ACE inhibitors and diuretics have been used successfully in combination. Nitrates are enodilators, which reduce cardiac volumes and filling pressures. In theory, nitrates can reduce pulmonary edema without reducing blood pressure, but patients develop tolerance to the drugs. Therefore, their use should be reserved for patients with angina or high preload levels, and some clinicians advocate periods when the patient is off nitrates.

What is the role of digitalis?

Digitalis' popularity has waxed and waned over the years. Digitalis improves cardiac contractility (it is a positive inotrope), reduces the activity of the sympathetic nervous system, and reduces activity of the renin-angiotensin system in patients with systolic dysfunction. It has clear benefits in the management of atrial fibrillation associated with CHF. Unfortunately, in heart failure its benefits may be offset by an increased incidence of drug-induced arrhythmias. It remains unclear whether digitalis has a role in managing patients with CHF who are in sinus rhythm. A number of studies are frequently cited as providing support for the use of digitalis in such patients, in the presence of systolic dysfunction, as an adjunct to other standard therapy. Two large randomized trials (PROVD and RADIANCE) reported better outcomes in patients treated with digitalis than in those receiving placebos;[26-28] furthermore, the benefits found in these studies seemed to accrue with low doses, which would theoretically minimize the incidence of arrhythmias.[29] In both studies, however, all subjects were already receiving chronic digitalis therapy at the time of enrollment, which biases the results. Digitalis has not been shown to reduce mortality, but it does result in a decrease in hospitalization.[30]

Are other drugs important for patients with heart failure?

Positive inotropes such as enoximone and vesnarinone, and antiarrythmics such as amiodarone seem to increase exercise tolerance or other quality-of-life measures, but are not associated with increased survival and may actually decrease survival. While such drugs cannot be generally recommended, there may be individual patients for whom the trade-off of a shortened length of survival in return for an increased quality of life in the short term may represent an attractive choice.[31]

Is there a role for positive inotropes?

A number of positive inotropic agents (phosphodiesterase inhibitors and dopamine agonists), which first met with great enthusiasm, have now fallen into disfavor. Even though they acutely increase cardiac output and improve hemodynamics, thus producing an associated short-term improvement in symptoms, they seem to accelerate the underlying problem, leading to more rapid deterioration and earlier mortality. Enoximone, a cyclic adenosine monophosphate phosphodiesterase inhibitor, has been touted as increasing exercise tolerance. A double-blind RCT showed that while it did increase some aspects of quality of life, the effect was transient and treatment was associated with increased mortality.[32] An RCT of vesnarinone suggested it offered benefit at low doses but was harmful at higher doses. Given the narrow therapeutic-to-toxic ratio, this drug is not destined for routine use.[33] Milrinone, a phosphodiesterase inhibitor, resulted in an increased mortality in patients with severe heart failure, possibly due to a proarrhythmic effect.[34, 35]

Is there a role for antiarrhythmics?

Because about half of all deaths in CHF are sudden deaths, there is great interest in the use of antiarrythmics in these patients, despite the potentially proarrhythmic effects known to occur with chronic use of such agents. Most of the attention has centered on amiodarone, a very effective Class IV antiarrhythmic, but one with a prominent side-effect profile when used in "standard" doses. Use of lower daily doses, such as 300 mg per day, however, seems

to maintain efficacy and diminish many of the major adverse effects.

A recent RTC followed patients with EF less than 35% and asymptotic ventricular arrhythmias. The study compared patients given amiodarone with those given no anti-arrhythmic. There was some benefit, but the numbers were small and several patients dropped out of the study.[36] Another RCT from the Veterans Administration system involving patients taking higher doses came to a different conclusion. Despite effective suppression of ventricular arrhythmia and improved LVED, amiodarone did not decrease mortality.[37] Finally, a meta-analysis of 13 studies with over 6,000 total patients found a relatively small benefit with the drug (a 13% relative decrease in overall mortality, due mostly to a 29% relative decrease in sudden death), but at the cost of a small (1%) absolute increase in pulmonary toxicity. In summary, there does appear to be some benefit of low-dose amioderone, but the overall impact on mortality will likely be small given the poor overall health of heart failure patients.[38]

In summary, while nearly half of all deaths in heart failure patients are due to sudden lethal arrhythmias, and the use of anti-arrhythmic drugs would seem to make sense, the data have not supported their use. Multiple methods have been suggested, however, to assess prognosis and intervene to improve survival. The firmest evidence comes from the more than two dozen studies that have suggested a substantial reduction in mortality by using ACE inhibitors.[39]

Is there anything else I can provide for Mr. G?

Mr. G. needs to be educated about his disease and its prognosis, including its progressively worsening course. Patients should be told about the crucial role of exercise to enhance functional status and quality of life (but apparently not length of life). Patients may do better when they are given anticipatory counseling, discussing what symptoms to expect and how to treat them, the benefits of regular exercise, the importance of a low salt diet, the need to take medicines as directed, and issues related to a durable power of attorney. The prognosis for this disease remains poor. The 12-month mortality is estimated at nearly 50%, underscoring the need to raise end-of-life issues with patients. Researchers from the SUPPORT study interviewed nearly 1,000 patients hospitalized with a exacerbation of heart failure. Nearly one-quarter (23%) indicated that they did not wish to be resuscitated in the event of a cardiac arrest. Yet only 25 of study participants ever discussed the topic with their physicians. Physicians were unable to predict their patients' preferences.

Mr. G. is placed on an ACE inhibitor, a beta blocker, and cholesterol-lowering medication. He has started cardiac rehabilitation and has met several times with the cardiac dietitian. He has been educated about how to take his medication and how to use his bathroom scale to monitor his fluid status.

Is Mr. G. now ready for discharge?

According to AHCPR, Mr. G. should be discharged from the hospital when:

- **Symptoms of heart failure have been adequately controlled.**
- **All reversible causes of morbidity have been treated or stabilized.**
- **Family/caregivers have been educated about medications, diet, activity and exercise recommendations, and symptoms of worsening heart failure.**
- **Adequate outpatient support and follow-up care have been arranged.**

During the past decade, the length of stay for elderly patients has decreased by 18%.[40] For many conditions there has been a concomitant increase in readmission rates. Several studies over the past few years have documented the enormous benefit to patients (quality of life) and society (reduced costs) associated with a greater use of multidisciplinary home care services. Researchers at the University of Pennsylvania looked at whether a multidisciplinary intervention could decrease readmission rates (and costs associated with readmission). Patients were assigned to either routine or comprehensive discharge planning. Those who received the nurse-administered comprehensive discharge planning (education, referrals, telephone monitoring of status, etc.) fared better, with fewer hospitalizations.[40-42]

Researchers at Kaiser have shown that a nurse-mediated system of aftercare, including diet education (reduced sodium intake), regular telephone monitoring, and feedback to the primary care physician improved clinical outcomes and reduced costs.[43] The results of the study have been confirmed by several other groups, including Veterans Administration patients[44] and others.[45,46] It thus seems quite reasonable for heart failure patients to assure that, prior to discharge, arrangements have been made for close follow-up, patient education, and instructions concerning medication compliance and interventions required if conditions worsen. When dedicated groups of physicians and nurse practitioners provided care, including behavior modification, exercise interventions, and dietary counseling, compliance with medications increased, feelings of well-being improved, and emergency room visits and hospital admissions decreased.[47]

Patients like Mr. G., hospitalized for heart failure, should be seen or contacted within 1 week of discharge, to make sure that they are stable in the outpatient setting and to check their understanding of and compliance with the treatment plan.

Key Clinical Points

- A minority of patients with heart failure are receiving ACE inhibitors—the only class of drugs proven to decrease mortality
- Beta blockers can have a beneficial effect when used in patients with mild to moderate heart failure, started early, titrated up slowly, and monitored closely to allow withdrawal in the presence of significant adverse outcomes
- Patient education about lifestyle changes, prognosis, and issues related to quality of life and end of life are as important as choosing the proper medications

References

1. Sharpe, N, Doughty R. Epidemiology of heart failure and ventricular dysfunction, *Lancet* 1998; 352(suppl 1):3-7.
2. Luzier AB, et al. Impact of angiotensin-converting enzyme inhibitor underdosing on rehospitalization rates in congestive heart failure. *Am J Card.* 1998; 82:465.
3. Gartis WA, et al. Is optimal angiotensin-converting enzyme inhibitor dosing neglected in elderly patients with heart failure? *Am Heart J.* 1998; 136:43.
4. Clark AL, et al. Severity of heart failure and dosage of angiotensin converting enzyme inhibitors. *Br Med J.* 1995; 310:973.
5. Mendelson G, et al. Underutilization of angiotensin-converting enzyme inhibitors in older patients with q-wave anterior myocardial infarction in an academic hospital-based geriatrics practice. *J Am Ger Soc.* 1998; 46:751.
6. Stafford RS, et al. National parterns of angiotensin-converting enzyme inhibitor use in congestive heart failure. *Arch Intern Med.* 1997; 157:2460.
7. Bart BA, et al. Reasons for underuse of angiotensin-converting enzyme inhibitors in patients with heart failure and left ventricular dysfunction. *Am J Card.* 1997; 79:1118.
8. Philbin EF, et al. Patterns of angiotensin-converting enzyme inhibitor use in congestive heart failure in two community hospitals. *Am J Card.* 1996; 77:832.
9. Cleland JGF, Swedberg K, Poole-Wilson PA. Successes and failures of current treatment of heart failure. *Lancet* 1998; 352(suppl 1):19-28.
10. Hall D, et al. Counteraction of the vasodilator effects of enalapril by aspirin in severe heart failure. *J Am Coll Cardiol.* 1992; 20:1549.
11. Cleland JGF, et al. Is aspirin safe for patients with heart failure? *Br Heart J.* 1995; 75:215.
12. Heerdink ER, et al. NSAIDs associated with increased risk of congestive heart failure in elderly patients taking diuretics. *Arch Intern Med.* 1998; 158:1108.
13. Haque WA, et al. Hemodynamic effects of supplemental oxygen administration in congestive heart failure. *J Am Coll Card.* 1996; 27:353.
14. Bersten AD, et al. Treatment of severe cardiogenic pulmonary edema with continuous positive airway pressure delivered by face mask. *N Engl J Med.* 1991; 325:1825.
15. Bradley TD, et al. Cardiac output response to continuous positive airway pressure in congestive heart failure. *Am Rev Resp Dis.* 1992; 145:377.
16. Baratz DM, et al. Effect of nasal continuous positive airway pressure on cardiac output and oxygen delivery in patients with congestive heart failure. *Chest.* 1992; 102:1397.
17. Dormans TPJ, et al. Diuretic efficacy of high dose furosemide in severe heart failure: Bolus injection versus continuous infusion. *J Am Coll Card.* 1996; 28:376.
18. The CIBIS II Investigators and Commirtees. The cardiac insufficiency bisoprolol study II: a randomized trial. *Lancet* 1999; 353:9-13.
19. Sackner-Bernstein JD, et al. Rationale for treatment of patients with chronic heart failure with adrenergic blockade. *JAMA.* 1995; 274:1462.
20. Aronow WS, et al. Effect of propranolol versus no propranolol on total mortality plus nonfatal myocardial infarction in older patients with prior myocardial infarction, congestive heart failure, and left ventricular ejection fraction 4% or higher treated with diuretics plus angiotensin-converting enzyme inhibitors. *Am J Card.* 1997; 80:207.
21. Vantrimpont P, et al. Additive beneficial effects of beta-blockers to angiotensin-converting enzyme inhibitors in the survival and ventricular enlargement (SAVE) study. *J Am Coll Card.* 1997; 29:229.
22. Paolisso G, et al. Metabolic and cardiovascular benefits deriving from beta-adrenergic blockade in chronic congestive heart failure. *Am Heart J.* 1992; 123:103.
23. Packer M, et al. The effect of carvedilol on morbidity and mortality in patients with chronic heart failure. *N Engl J Med.* 1996; 334:1349.
24. Packer M, et al. Double-blind, placebo-controlled study of the effects of carvedilol in patients with moderate to severe heart failure: The precise trial. *Circulation.* 1996; 94:2793.
25. Cleland JGF, McGowen J, Clark A, Freemantle, N. The evidence for beta blockers in heart failure. *BMJ* 1999; 318:824-825.
26. Tauke J, et al. Digoxin for chronic heart failure: A review of the randomized controlled trials with special attention to the proved and radiance trials. *Prog Cardiovasc Dis.* 1994; 37:49.
27. Adams, KF, et al. Patients with mild heart failure worsen during withdrawal from digoxin therapy. *J Am Coll Card.* 1997; 30:42.
28. Packer M, et al. Withdrawal of digoxin from patients with chronic heart failure treated with angiotensin-converting-enzyme inhibitors. *N Engl J Med.* 1993; 329:1.
29. Slatton ML, et al. Does digoxin provide additional hemodynamic and autonomic benefit at higher doses in patients with mild to moderate heart failure and normal sinus rhythm? *J Am Coll Card.* 1997; 29:1206.
30. The Digitalis Investigation Group. The effect of digoxin on mortality and morbidity in patients with heart failure. *N Engl J Med.* 1997; 336:525.
31. Hampton JR. Prime II: Another disappointment in heart failure therapy. *Eur Heart J.* 1997; 18:1519.
32. Cowley AJ, et al. Treatment of severe heart failure: quantity or quality of life? *Br Heart J.* 1994; 72:226.
33. Feldman AM, et al. Effects of vesnarinone on morbidity and mortality in patients with heart failure. *N Engl J Med.* 1993; 329:149.
34. Packer M, et al. Effect of oral milrinone on mortality in severe chronic heart failure. *N Engl J Med.* 1991; 325:1468.
35. Anderson JL, et al. Hemodynamic and clinical benefits with intravenous milrinone in severe chronic heart failure: results of a multicenter study in the United States. *Am Heart J.* 1991; 121:1956.
36. Garguichevich JJ, et al. Effect of amiodarone therapy on mortality in patients with left ventricular dysfunction and asymptomatic complex ventricular arrhythmias: Argentine pilot study of sudden death and amiodarone (EPAMSA). *Am Heart J.* 1995; 130:494.
37. Singh, SN, et al. Amiodarone in patients with congestive heart failure and asymptomatic ventricular arrhythmia. *N Engl J Med.* 1995; 333:77.
38. Amiodarone Trials Meta-Analysis Investigators. Effect of prophylactic amiodarone on mortality after acute myocardial infarction and in congestive heart failure: Meta-Analysis of individual data from 6500 patients in randomised trials. *Lancet.* 1997; 350:1417.
39. Feldman AM. Can we alter survival in patients with congestive heart failure? *JAMA.* 1992; 267:1956.
40. Naylor M, et al. Comprehensive discharge planning for the hospitalized elderly: A randomized clinical trial. *Ann Intern Med.* 1994; 120:999.
41. Shah NB, et al. Prevention of hospitalizations for heart failure with an interactive home monitoring program. *Am Heart J.* 1998; 135:373.
42. Krumholz HM, et al. Readmission after hospitalization for congestive heart failure among medicare beneficiaries. *Arch Intern Med.* 1997; 157:99.
43. West JA, et al. A comprehensive management system for heart failure improves clinical outcomes and reduces medical resource utilization. *Am J Card.* 1997; 79:58.
44. Weinberger M, et al. Does increased access to primary care reduce hospital readmissions? *N Engl J Med.* 1996; 334:1441.
45. Rich MW, et al. A multidisciplinary intervention to prevent the readmission of elderly patients with congestive heart failure. *N Engl J Med.* 1995; 333:1190.
46. Rich MW, et al. Prevention of readmission in elderly patients with congestive heart failure: Results of a prospective, randomized pilot study. *J Gen Intern Med.* 1993; 8:585.
47. Krum H, Reducing the burden of chronic heart failure: It's time to adopt new management strategies. *Med J Australia.*1997; 167:61.

CLINICAL EVIDENCE

Genital herpes

This article comes from *Clinical Evidence*, a new resource for clinicians produced jointly by the BMJ Publishing Group and the American College of Physicians–American Society of Internal Medicine. *Clinical Evidence* is an extensively peer reviewed publication that summarizes the best available evidence on the effects of common clinical interventions gleaned from thorough searches and appraisal of the world literature. The first issue is available in book form in the UK in June with a US version planned for publication in October. The second issue will be updated and expanded to cover more topics and questions and will be published six months later. Please see the advertisement for more information or alternatively visit our Web site at www.evidence.org.

Anna Wald
Department of medicine and epidemiology
University of Washington Virology Research Clinic
1001 Broadway, Suite 320
Seattle, WA 98122

annawald@u.washington.edu

QUESTIONS: What are the effects of antiviral treatment on a first episode of genital herpes? Which interventions reduce the impact of recurrent genital herpes? Which interventions prevent transmission of herpes simplex virus?

INTERVENTIONS

Beneficial

Oral antiviral treatment during the first episode
Oral antiviral treatment taken at the start of a recurrence
Daily oral antiviral treatment in people with high rates of recurrence

Likely to be beneficial

Daily oral antiviral treatment in late pregnancy in women with a history of genital herpes

Unknown effectiveness

Psychotherapy
Interventions to prevent sexual transmission
Cesarean section in women with genital lesions at term
Serological screening and counseling in late pregnancy

Key Clinical Points

- Evidence from randomized controlled trials (RCTs) shows that oral antiviral treatment reduces the duration of symptoms, lesions, and viral shedding in first and recurrent episodes of genital herpes and that daily treatment reduces the rate of recurrence
- Evidence from RCTs shows no significant difference in effectiveness or adverse effects between acyclovir (aciclovir), valaciclovir, and famciclovir
- Interventions to prevent sexual transmission have not yet been adequately assessed in RCTs
- The highest risk of mother-to-baby transmission is among women who are newly infected with genital herpes in late pregnancy. Interventions aimed at preventing infection in late pregnancy (such as serological screening and counseling) have not been evaluated.
- The effect of cesarean section on mother-to-baby transmission has not been evaluated. The procedure carries the risk of excess maternal morbidity and mortality
- Limited evidence from RCTs suggests that antiviral treatment may reduce the number of pregnant women with genital lesions at term. Since women with genital lesions at term are usually offered cesarean sections, antiviral treatment may reduce the rate of cesarean sections

Definition

Genital herpes is the result of an infection with herpes simplex virus type 1 or 2 (HSV-1 or HSV-2), which causes ulceration in the genital area. HSV infections can be classified on the basis of virological and serological findings. Types of infection include: first-episode primary infections (HSV in a person without evidence of previous infection—that is, no antibodies to HSV-1 or HSV-2); first-episode non-primary infections (HSV-2 in a person who previously had antibodies to HSV-1); and first recognized recurrence of HSV-2 or HSV-1 in a person who previously had antibodies to HSV-2 or HSV-1. Recurrent genital herpes is caused by reactivation of latent HSV.

Prevalence

Genital herpes infections are among the most common sexually transmitted diseases. Seroprevalence studies show that 22% of adults in the United States have HSV-2 infection[1]; a U.K. study showed that 23% of adults attending sexual medicine clinics and 7.6% of blood donors in London had antibodies to HSV-2.[2]

Etiology

Both HSV-1 and HSV-2 can cause a first episode of genital infection, but HSV-2 is more likely to cause recurrent disease.[3] Most people with HSV-2 infections are not aware that they have genital herpes, as their symptoms are mild. However, these people serve as a source of new infections for sexual partners and newborns.[4,5]

Prognosis

The sequelae of HSV infection include neonatal HSV, opportunistic infections in immunocompromised people,

recurrent genital ulceration, and psychosocial morbidity. HSV-2 infection is associated with an increased risk of HIV transmission and acquisition. The commonest neurological complications are aseptic meningitis (reported in about a quarter of women during primary infection) and urinary retention. The risk of neonatal infection is high (41%, 95% CI 26% to 56%) in babies born to women who acquire infection near the time of labor[6,7] and low (<3%) in women with established infection, even in those who have a recurrence at term. About 15% of neonatal infections result from postnatal transmission from oral lesions.

Aims

To reduce the morbidity of the first episode, to reduce the risk of recurrent disease after a first episode, and to prevent further transmission.

Outcomes

Severity and duration of symptoms, healing time, duration of viral shedding, rates of recurrence, psychosocial morbidity, rates of transmission, adverse effects of treatment

Methods

Medline was searched for articles published from 1992 to 1998 using the terms herpes simplex virus, valaciclovir, famciclovir, cidofovir, trifluridine, and neonatal herpes. Preliminary results of clinical trials published in the abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy and the International Society for STD Research were also included. Experts in the field, as well as makers of antiviral drugs, were contacted to identify completed studies which were undergoing peer review but had not yet been published.

QUESTION: What are the effects of antiviral treatment on a first episode of genital herpes?

Evidence from RCTs shows that oral antiviral treatment decreases the duration of lesions, symptoms, and viral shedding and prevents neurological complications in patients with first-episode genital herpes. It is more convenient than intravenous treatment and more effective than topical treatment. Limited data provide no evidence that oral antiviral treatment reduces the rate of recurrence compared with placebo. Evidence from RCTs shows no significant difference between acyclovir (aciclovir), valaciclovir, and famciclovir.

Benefits

No systematic review

Immediate effects

We found several RCTs (>350 men and women) of oral acyclovir (aciclovir) for the treatment of first-episode genital herpes. Compared with placebo, acyclovir 200 mg 5 times a day decreased the duration of viral shedding (2 vs 10 days), pain (5 vs 7 days), and time to healing of lesions (8 vs 14 days) and prevented formation of new lesions. Neurological complications (aseptic meningitis and urinary retention) were also reduced. Numbers were small, so no firm estimates of effectiveness were available.[8-12]

Different regimens

In an international trial of 643 healthy adults with first-episode genital herpes, valaciclovir 1000 mg twice daily was compared with acyclovir 200 mg 5 times a day for 10 days.[13] No significant differences were noted between the 2 drugs in any clinical or virological variables. Another RCT evaluated 3 different doses of famciclovir (125 mg, 250 mg, or 500 mg 3 times a day) versus acyclovir 200 mg 5 times a day in 951 adults with first-episode genital herpes.[14] No significant differences were found.

Recurrence rates

A meta-analysis of 2 placebo-controlled RCTs in 61 participants showed no significant difference in time to recurrence or frequency of recurrence between those given acyclovir and those given placebo.[15]

Harms

Adverse effects (mostly headache and nausea) were rare and occurred with similar frequency on acyclovir (aciclovir), valaciclovir, famciclovir, and placebo.

Comment

Intravenous and topical acyclovir have also been studied. Oral acyclovir is more convenient than intravenous and more effective than topical preparations.[16]

QUESTION: Which interventions reduce the impact of recurrent genital herpes?

OPTION: ANTIVIRAL TREATMENT AT THE START OF RECURRENCE

Evidence from RCTs shows that oral antiviral treatment taken at the start of recurrence reduces the duration of lesions, symptoms, and viral shedding in patients with recurrent genital herpes.

Benefits

No systematic review. Several RCTs in >650 healthy adults with recurrent genital herpes were identified in a nonsystematic review published in 1990.[17] These evaluated 5 days of oral acyclovir 200 mg 5 times a day or 800 mg twice a

day initiated at the first sign of recurrence. Compared with placebo, treatment decreased viral shedding (1 vs 2 days) and duration of lesions (5 vs 6 days). An RCT in 739 people with recurrent genital herpes compared patient-initiated valaciclovir 500 mg or 1000 mg twice daily for 5 days with placebo. Valaciclovir decreased the duration of episodes (4 vs 6 days), reduced viral shedding (2 vs 4 days), and increased the rate of aborted recurrences (31% vs 21%).[18] An RCT of famciclovir (125 to 500 mg twice daily) versus placebo in 467 people with recurrent genital herpes found a significant reduction in the duration of lesions (5 vs 4 days) and viral shedding (3 vs 2 days).[19] Differences were significant for all doses of famciclovir (P<0.01). Two RCTs in 1939 patients found no significant difference between valaciclovir and acyclovir.[20, 21]

Harms

Adverse effects (mostly headache and nausea) were rare and occurred with similar frequency during treatment with acyclovir, valaciclovir, famciclovir, and placebo.

Comment

The benefit was greater if the patient initiated treatment at the first symptom or sign of recurrence.[22] People with recurrent herpes can learn to recognize recurrences early and should have an adequate supply of medicine at home.

OPTION: DAILY MAINTENANCE ANTIVIRAL TREATMENT

Evidence from RCTs shows that daily maintenance treatment with oral antiviral agents reduces the frequency of recurrences and viral shedding in patients with genital herpes. Daily treatment may also improve psychosocial function.

Benefits

No systematic review

Recurrence rates

Several RCTs were identified in a nonsystematic review published in 1990.[17] These compared daily treatment with varying doses of acyclovir versus placebo for prevention of recurrences in people with genital herpes. Most participants had a history of frequent recurrences (6 or more each year). Daily acyclovir reduced the recurrence rate by 74% to 93%, and recurrences were shorter than those that occurred without treatment (3.5 vs 5 days).[17] Of 210 adults who completed 5 years of continuous treatment with acyclovir 400 mg twice daily, 53% to 70% were free of recurrence each year.[23]

The first year of this study was a double-blind, placebo-controlled RCT in 1146 adults. Those on acyclovir had significantly fewer recurrences during the first year (1.7 vs 12.5, P<0.0001). Two RCTs evaluated daily valaciclovir.[24, 25] In a 1 year study of 479 adults, 40% to 50% of people who received valaciclovir 500 mg or 1000 mg once daily, valaciclovir 250 mg twice daily, or acyclovir 400 mg twice daily were free from recurrence, compared with 5% of people who received placebo.

Two RCTs evaluated daily famciclovir for up to 1 year in adults with frequently recurring genital herpes.[26, 27] In a 1-year study of 455 adults treated with varying doses of famciclovir, the median time to first recurrence was 11 months for famciclovir 250 mg twice daily and 1.5 months for placebo.

Viral shedding

One RCT has evaluated the effect of daily maintenance treatment on viral shedding in women with recently acquired genital HSV-2 infection. Participants provided swabs for viral cultures daily for 70 days while receiving acyclovir 400 mg twice daily or placebo.[28] Viral shedding was reduced by 95% on days with reported lesions and by 94% on days without lesions.

Psychosocial morbidity

There were no RCTs that assessed this outcome. The effect of daily acyclovir on psychosocial morbidity has been assessed in a prospective observational study of 102 men and women with frequently recurring genital herpes.[29] Patients were questioned to assess their mental health and psychosocial functioning. Levels of anxiety and depression fell from 63% to 26% in 80% of patients who completed 3 months of acyclovir treatment.

Harms

Daily treatment with acyclovir, famciclovir, and valaciclovir was well tolerated. Patients on acyclovir have been followed for up to 7 years and on famciclovir and valaciclovir for up to 1 year. Nausea and headache were infrequent, and patients rarely discontinued treatment because of adverse effects. Whether daily maintenance treatment increases high-risk sexual behavior has not been studied. There is no evidence that daily treatment with acyclovir results in the emergence of acyclovir-resistant HSV during or after cessation of treatment in healthy adults.[30]

Comment

Although continuous treatment is safe, discussion of cessation of treatment is reasonable on an annual basis, as some patients experience less frequent recurrences with time or experience less distress during the recurrences. Several effective dosages have been studied: most patients prefer regimens of once- or twice-daily doses. Patients with frequent recurrences may benefit from twice-daily treatment.

OPTION: PSYCHOTHERAPY

The effects of psychotherapy on the rate of recurrence of genital herpes have not yet been adequately studied.

Benefits

A systematic review published in 1993 identified 6 studies of psychotherapeutic interventions in 69 participants (4 studies had <10 participants).[31] Interventions varied from hypnotherapy and progressive muscle relaxation to cognitive therapy and multidimensional psychosocial intervention. In the largest study, 31 patients with 4 or more recurrences each year were randomly allocated to treatment with psychosocial intervention, social support, or a place on a waiting list. Participants receiving psychosocial intervention had significantly lower recurrence rates (6 per year) compared with the pretreatment frequency (11 per year) and with the other groups (11 per year).

Harms

No adverse effects were noted.

Comment

Small numbers of patients, inadequate controls, and subjective and retrospective assessment of recurrence frequency at baseline limit the usefulness of these studies. Controlled studies that include prospective clinical evaluation of disease activity are needed.

QUESTION: Which interventions prevent transmission of HSV?

OPTION: CONDOMS, ANTIVIRAL TREATMENT, IMMUNIZATION

The effectiveness of these interventions in preventing HSV transmission has not been adequately studied.

Condoms

No RCTs. In a prospective cohort study of 144 couples in the United States discordant for HSV-2 infection, use of condoms or diaphragms was associated with a lower rate of HSV-2 acquisition, 5.7% versus 13.6% (P=0.2).[32]

Antiviral treatment

No RCTs have looked at rates of transmission. RCTs have shown, however, that daily antiviral treatment decreases the frequency of clinical and subclinical viral shedding (see above). There is no direct evidence that treatment reduces HSV transmission in serologically discordant couples.

Immunization

No effective vaccines are currently available.

Harms

The same as for individual interventions

Comment

Controlled studies of condoms for the prevention of HSV-2 transmission are unlikely to be done. As HSV reactivates over a wide genital area, condoms may offer less protection against genital herpes than for STDs characterized by urethral or cervical discharge.

OPTION: CESAREAN SECTION

The effect of Cesarean section on the risk of neonatal herpes is uncertain. The procedure carries the risk of excess maternal morbidity and mortality.

Benefits

No RCTs have assessed the benefits of Cesarean section. In the Netherlands, women with recurrent genital herpes at delivery have been allowed vaginal birth since 1987. This policy has not resulted in an increase of neonatal herpes: 26 cases occurred from 1981 to 1986 and 19 cases from 1987 to 1991.[7]

Harms

Cesarean sections are associated with significant maternal morbidity and mortality. The number of maternal deaths caused to prevent 1 neonatal death from HSV has been estimated as 0.57.[33] The estimated cost of the excess of cesarean sections is $2.5m per case of neonatal HSV averted.

Comment

Countries vary in their approach to the obstetric management of women with recurrent genital herpes at delivery. Women with genital lesions at term have Cesarean sections in the United States and in the United Kingdom, with attendant maternal and financial costs. The risk of neonatal infection is high (41%, 95% CI 26% to 56%) in babies born to women who acquire their infection near the time of labor[6,7] and low (<3%) in women with established infection, even in those who have a recurrence at term. Most women who acquire infection toward the end of pregnancy are undiagnosed, and most cases of neonatal HSV infection are acquired from women without a history of genital herpes. The available evidence suggests that prevention of neonatal HSV should focus on preventing infection in late pregnancy.

OPTION: ANTIVIRAL TREATMENT DURING PREGNANCY

There is limited evidence from a systematic review of RCTs that acyclovir reduces the rate of cesarean section in women with first or recurrent episodes of genital HSV

during pregnancy. The risk of rare adverse events has not been adequately studied.

Benefits

A systematic review published in 1998 identified 3 studies, including 2 RCTs, of daily acyclovir versus placebo in 210 near-term pregnant women with genital herpes.[7] The dose and duration of acyclovir and the populations enrolled differed in each study. Cesarean section was performed in women with genital lesions at labor. All 3 studies found lower rates of Cesarean section in women treated with acyclovir: 8% versus 34% (P=0.02), 13% versus 33% (P=0.03) and 13% versus 25% (P=0.2).

Harms

No adverse effects for women or newborns were reported.

Comment

The number of women was small, and rare events, such as an increase in asymptomatic viral shedding or acyclovir-related obstructive uropathy in the newborns, would be difficult to detect.

OPTION: SEROLOGICAL SCREENING AND COUNSELING DURING PREGNANCY

Neither serological screening with type-specific assays to identify women at risk for HSV acquisition in late pregnancy nor counseling to avoid genital-genital and oral-genital contact in late pregnancy has been evaluated.

This paper will be published in *Clinical Evidence* in June 1999. Information about the journal is available on www.evidence.org.

References

1. Fleming DT, McQuillan GM, Johnson RE, et al. Herpes simplex virus type 2 in the Unired Srates, 1976 to 1994. N Engl J Med 1997; 337:1105-11.
2. Cowan FM, Johnson AM, Ashley R, Corey L, Mindel A. Anribody ro herpes simplex virus type 2 as serological marker of sexual lifestyle in populations. *BMJ* 1994; 309:1325-9.
3. Benedetti J, Corey L, Ashley R. Recurrence rates in geniral herpes after symptomatic firsr-episode infection. *Ann Intern Med* 1994; 121:847-54.
4. Mertz GJ, Schmidt O, Jourden JL, et al. Frequency of acquisition of first-episode genital infection with herpes simplex virus from symptomatic and asympromatic source contacts. *Sex Transm Dis* 1985; 12:33-9.
5. Whitley RJ, Kimberlin DW, Roizman B. Herpes simplex viruses. *Clin Infect Dis* 1998; 26:541-53; 554-5.
6. Brown ZA, Selke SA, Zeh J, et al. Acquisition of herpes simplex virus during pregnancy. *N Engl J Med* 1997; 337:509-15.
7. Smith J, Cowan FM, Munday P. The management of herpes simplex virus infection in pregnancy. *Br J Obstet Gynaecol* 1998; 105:255-68.
8. Nilsen AE, Aasen T, Halsos AM, et al. Efficacy of oral acyclovir in trearment of initial and recurrent genital herpes. *Lancet* 1982; 2:571-3.
9. Corey L, Fife K, Benedetti JK, et al. Intravenous acyclovir for the treatment of primary genital herpes. *Ann Intern Med* 1983; 98:914-21.
10. Mertz G, Critchlow C, Benedetti J, et al. Double-blind placebo-conrrolled rrial of oral acyclovir in the first episode of genital herpes simplex virus infection. *JAMA* 1984; 252:1147-51.
11. Mindel A, Adler MW, Sutherland S, Fiddian AP. Intravenous acyclovir treatment for primary genital herpes. *Lancet* 1982; 1:697-700.
12. Bryson YJ, Dillon M, Lovett M, et al. Treatment of first episodes of genital herpes simplex virus infections with oral acyclovir: a randomized double-blind controlled trial in normal subjects. *N Engl J Med* 1983; 308:916-20.
13. Fife KH, Barbarash RA, Rudolph T, Degregorio B, Roth R. Valaciclovir versus acyclovir in the treatment of first-episode genital herpes infection: results of an international, multicenter, double-blind randomized clinical trial. *Sex Transm Dis* 1997; 24:481-6.
14. Loveless M, Harris W, Sacks S. Treatment of first episode genital herpes wirh famciclovir. *Programs and abstracts of the 35th Interscience Conference on Antimicrobial Agents and Chemotherapy.* San Francisco, CA, 1995.
15. Corey L, Mindel A, Fife KH, Sutherland S, Benederti J, Adler MW. Risk of recurrence after treatment of first episode genital herpes with inrravenous acyclovir. *Sex Trans Dis* 1985; 12:215-8.
16. Corey L, Benederri J, Crirchlow C, et al. Treatment of primary first-episode genital herpes simplex virus infections with acyclovir: results of topical, intravenous and oral therapy. *J Antimicrob Chemother* 1983; 12(suppl B):79-88.
17. Srone K, Whittington W. Treatment of genital herpes. *Rev Infect Dis* 1990; 12(suppl 6):S610-9.
18. Spruance S, Trying S, Degregorio B, et al. A large-scale, placebo-controlled, dose-ranging trial of peroral valacyclovir for episodic treatment of recurrent herpes genitalis. *Arch Intern Med* 1996; 156:1729-35.
19. Sacks SL, Aoki FY, Diaz-Mitoma F, Sellors J, Shafran SD. Patient-initiated, twice-daily oral famciclovir for early recurrent genital herpes: a randomized, double-blind mulricenter trial. *JAMA* 1996; 276:44-9.
20. Bodsworth NJ, Crooks RJ, Borelli S, et al. Valaciclovir versus acyclovir in patient-initiated treatment of recurrent genital herpes: a randomized, double-blind clinical trial. *Genitourin Med* 1997; 73:110-6.
21. Tyring SK, Douglas JM, Spruance SL, er al. A randomized, placebo-controlled comparison of oral valacyclovir and acyclovir in immunocompetent patients with recurrent genital herpes infections. *Arch Dermatol* 1998; 134:185-91.
22. Reichman RC, Badger GJ, Mertz GJ, et al. Treatment of recurrent genital herpes simplex infections wirh oral acyclovir: a conrrolled trial. *JAMA* 1984; 251:2103-7.
23. Goldberg L, Kaufman R, Kurtz T, et al. Continuous five-year treatment of patients with frequenrly recurring genital herpes simplex virus infection with acyclovir. *J Med Virol* 1993; S1:45-50.
24. Patel R, Bodsworth NJ, Wooley P, et al. Valaciclovir for the suppression of recurrent genital HSV infection: a placebo controlled study of once-daily therapy. *Genitourin Med* 1997; 73:105-9.
25. Reitano M, Tyring S, Lang W, et al. Valaciclovir for the suppression of recurrent genital herpes simplex virus infection: a large-scale dose range finding study. *J Infect Dis* 1998; 178:603-10.
26. Mertz GJ, Loveless MO, Levin MJ, et al. Oral famciclovir for suppression of recurrent genital herpes simplex virus infection in women: a multicenter, double-blind, placebo-controlled trial. *Arch Intern Med* 1997; 157:343-9.
27. Diaz-Mitoma F, Sibbald RG, Shafran SD. Oral famciclovir for the suppression of recurrent genital herpes: a randomized controlled rrial. *JAMA* 1998; 280:887-92.
28. Wald A, Zeh J, Barnum G, Davis LG, Corey L. Suppression of subclinical shedding of herpes simplex virus type 2 with acyclovir. *Ann Intern Med* 1996; 124:8-15.
29. Carney O, Ross E, Ikkos G, Mindel A. The effect of suppressive oral acyclovir on the psychological morbidity associated with recurrent genital herpes. *Genitourin Med* 1993; 69:457-9.
30. Fife KH, Crumpacker CS, Mertz GJ. Recurrence and resistance patterns of herpes simplex virus following cessation of 6 years of chronic suppression with acyclovir. *J Infect Dis* 1994; 169:1338-41.
31. Longo D, Koehn K. Psychosocial factors and recurrent genital herpes: a review of prediction and psychiatric treatment studies. *Int J Psychiatry Med* 1993; 23:99-117.
32. Mertz GJ, Benedetti J, Ashley R, Selke SA, Corey L. Risk facrors for the sexual transmission of genital herpes. *Ann Intern Med* 1992; 116:197-202.
33. Randolph A, Washington A, Prober C. Cesarean delivery for women presenting with genital herpes lesions. *JAMA* 1993; 270:77-82.

Developing clinical guidelines

The methods of guideline development should ensure that treating patients according to guidelines will achieve the outcomes that are desired. This article presents a combination of the literature about guideline development and the results of our combined experience in guideline development in North America and Britain. It considers the 5 steps in the initial development of an evidence-based guideline.

Paul G Shekelle
West Los Angeles Veterans Affairs Medical Center (111G)
11301 Wilshire Blvd
Los Angeles, CA
90073

Steven H Woolf
Health Services Research and Development Service
Department of Family Practice
Virginia Commonwealth University
Fairfax, VA 22033

Martin Eccles
Center For Health Services Research
University of Newcastle upon Tyne
Newcastle upon Tyne
NE2 4AA
United Kingdom

Jeremy Grimshaw
Health Services Research Unit
University of Aberdeen
Aberdeen AB9 2ZD
United Kingdom

Correspondence to:
Dr Shekelle
shekelle@rand.org

Identifying and refining the subject area of a guideline

Prioritizing topics

Guidelines can be developed for a wide range of subjects. Clinical areas can be concerned with conditions (abnormal uterine bleeding, coronary artery disease) or procedures (hysterectomy, coronary artery bypass surgery). Given the large number of potential areas, some priority setting is needed to select an area for guideline development. Potential areas can emerge from an assessment of the major causes of morbidity and mortality for a given population, uncertainty about the appropriateness of health care processes or evidence that they are effective in improving patient outcomes, or the need to conserve resources in providing care.

Refining the subject area

The topic for guideline development will usually need to be refined before the evidence can be assessed in order to answer exact questions. The usual way of refining the topic is through dialogue among clinicians, patients, and the potential users or evaluators of the guideline. Discussions about the scope of the guideline will also take place within the guideline development panel.

If the topic is not refined, the clinical condition or question may be too broad in scope. For example, a guideline on the management of diabetes could cover primary, secondary, and tertiary care elements of management and also multiple aspects of management, such as screening, diagnosis, dietary management, drug treatment, risk factor management, or indications for referral to a specialist. Though all of these legitimately could be dealt with in a guideline, the task of developing such a guideline would be considerable; therefore, a group to develop guidelines needs to be clear which areas are and are not within the scope of their activities. It is possible to develop guidelines that are both broad in scope and evidence-based; but to do so usually requires considerable time and money, both of which are frequently underestimated by inexperienced developers of evidence-based clinical practice guidelines.

One method of defining the clinical question of interest and also identifying the processes for which evidence needs to be collected and assessed is the construction of models or causal pathways.[1] A causal pathway is a diagram that illustrates the links between interventions of interest and the intermediate, surrogate, and health outcomes that the interventions are thought to influence. In designing the pathway, guideline developers make explicit the premises on which their assumptions of effectiveness are based and the outcomes (benefits and harms) that they consider important. This identifies the specific questions that must be answered by the evidence to justify conclusions of effectiveness and highlights gaps in the evidence for which future research is needed.

Summary Points

- Identifying and refining the subject area is the first step in developing a guideline
- Convening and running guideline development groups is the next step
- On the basis of systematic reviews, the group assesses the evidence about the clinical question or condition
- This evidence is then translated into a recommendation within a clinical practice guideline
- The last step in guideline development is external review of the guideline

Running guideline development groups

Setting up a guideline development project

To successfully develop a guideline, it may be necessary to convene more than 1 group. A project or management team could undertake the day-to-day running of the work, such as the identification, synthesis, and interpretation of relevant evidence; the convening and running of the guideline development groups; and the production of the resulting guidelines. An additional guideline development group would produce recommendations in light of the evidence or of its absence.

Group membership and roles

Group members—Identifying stakeholders involves identifying all of the groups whose activities would be covered by the guideline or who have other legitimate reasons for having input in the process. This is important to ensure adequate discussion of the evidence (or its absence) when developing the recommendations in the guideline. When presented with the same evidence, a single specialty group will reach different conclusions than a multidisciplinary group—the specialty group will be systematically biased in favor of performing procedures in which it has a vested interest.[2,3] For example, a group of vascular surgeons favored the use of carotid endarterectomy more than a mixed group of surgeons and medical specialists.[4] Individuals' biases may be better balanced in multidisciplinary groups, and such balance may produce more valid guidelines. Ideally, the group should have at least 6 but no more than 12 to 15 members; too few members limit adequate discussion and too many members make effective functioning of the group difficult. Under certain circumstances (for example, in guidelines for broad clinical areas), it may be necessary to trade off full representation against the requirement of having a functional group.

Roles—Roles required within guideline development groups are those of group member, group leader, specialist resource, technical support, and administrative support. Group members are invited to participate as individuals working in their field; their role is to develop recommendations for practice based on the available evidence and their knowledge of the practicalities of clinical practice.

Skills needed for guideline development

- Literature searching and retrieval
- Epidemiology
- Biostatistics
- Health services research
- Clinical experts
- Group process experts
- Writing and editing

The role of the group leader is to ensure that the group both functions effectively (the group process) and achieves its aims (the group task). The process is best moderated by someone who is familiar with (though not necessarily an expert in) the management of the clinical condition and the scientific literature yet is not an advocate. He or she stimulates discussion and allows the group to identify where true agreement exists but does not inject his or her own opinions in the process. This requires someone with both clinical skills and group process skills. Using formal group processes rather than informal ones in group meetings produces different and possibly better outcomes.[5-7]

Identifying and assessing the evidence

Identifying and assessing the evidence is best done by performing a systematic review. The purpose of a systematic review is to collect all available evidence, assess its potential applicability to the clinical question under consideration, inspect the evidence for susceptibility to bias, and extract and summarize the findings.

What sort of evidence?

Identifying the clinical questions of interest will help set the boundaries for admissible evidence (types of study design, year of publication, etc.). For example, questions of the efficacy of interventions usually mean that randomized, controlled trials should be sought, while questions of risk usually mean that prospective cohort studies should be sought.

Where to look for evidence?

The first step in gathering the evidence is to see if a suitable, recent systematic review has already been published. Searching the *Cochrane Library* will also identify relevant Cochrane review groups, which should also be contacted to see if a review is in progress.

If a current systematic review is not available, a computer search of Medline and EMBASE is the usual starting point, using search strategies tailored to appropriate types of studies (though such strategies have been validated only for randomized, controlled trials.[8] For example, randomized, controlled trials provide the best evidence to answer questions about the effectiveness of treatments, whereas prospective cohort studies generally provide the best evidence for questions about risk. The Cochrane Controlled Trials Register (part of the *Cochrane Library*) contains references to over 218,000 clinical trials that have been identified through database and hand searching; it should be examined early on in any review process. Checking the references in articles will show additional relevant articles not identified by the computer search, and having experts in the field examine the list of articles helps ensure that there are no obvious omissions. Additional

search strategies, including searches for articles published in languages other than English,[9-11] computer searches of specialized databases, hand searching of relevant journals, and searching for unpublished material will often yield additional studies, but the resources needed for such activities are considerable. The cost-effectiveness of various search strategies has not been established. It is best to match the scope of the search strategy to the available resources.

Assessing studies for relevance

Once studies have been identified, they are assessed for relevance to the clinical questions of interest and for bias.[12, 13] Screening for relevance is often possible from the abstract; it narrows the set of studies to those needing a more detailed assessment. Using explicit rather than implicit criteria should improve the reliability of the process.

Summarizing evidence

Data are extracted from the relevant studies on the benefits, the harms, and (where applicable) the costs of the interventions being considered. These data are usually presented in a form that allows the designs and results of studies to be compared. Where appropriate, meta-analysis can be used to summarize the results of multiple studies.

Categorizing evidence

Summarized evidence is categorized to reflect its susceptibility to bias. This is a shorthand method of conveying specific aspects of the evidence to a reader of the guideline. A number of such "strength of evidence" classification schemes exist, but empirical evidence exists only for schemes that categorize effectiveness studies by study design.[14, 15] The box shows a simple scheme for classifying the evidence that supports statements in practice guidelines and the strength of the recommendations. Guideline developers should use a limited number of explicit criteria, incorporating criteria for which there is explicit evidence.

Classification Schemes

Category of evidence:

- IA evidence for meta-analysis of randomized, controlled trials
- IB evidence from at least one randomized, controlled trial
- IIA evidence from at least one controlled study without randomization
- IIB evidence from at least one other type of quasi-experimental study
- III evidence from nonexperimental descriptive studies, such as comparative studies, correlation studies, and case-control studies
- IV evidence from expert committee reports or opinions or clinical experience of respected authorities, or both

Strength of recommendation:

- A directly based on category I evidence
- B directly based on category II evidence or extrapolated recommendation from category I evidence
- C directly based on category III evidence or extrapolated recommendation from category I or II evidence
- D directly based on category IV evidence or extrapolated recommendation from category I, II, or III evidence

Factors contributing to the process of deriving recommendations

- The nature of the evidence (for example, its susceptibility to bias)
- The applicability of the evidence to the population of interest (its generalizability)
- Costs
- Knowledge of the health care system
- Beliefs and values of the panel

Translating evidence into a clinical practice guideline

The evidence, once gathered, needs to be interpreted (see box). Since conclusive evidence exists for relatively few health care procedures, deriving recommendations solely from such examples would lead to developing a guideline of limited scope or applicability.[16] This could be sufficient if, for example, the guideline is to recommend the most strongly supported treatments for a given illness. More commonly, however, the evidence needs to be interpreted into a clinical, public health, policy, or payment context. Therefore, within the guideline development process, a decision should be made about how opinion will be both used and gathered.

Using and gathering opinion

Opinion will be used to interpret evidence and also to derive recommendations in the absence of evidence. When evidence is being interpreted, opinion is needed to assess issues such as the generalizability of the evidence—for example, to what degree evidence from small, randomized clinical trials or controlled observational studies may be generalized or to what degree results from a study in one population can be extrapolated to the population of interest in the guideline (for example, extrapolating a study from a tertiary, academic medical center to the community population of interest to potential users of the guideline).

Recommendations based solely on clinical judgment and experience are likely to be more susceptible to bias and self-interest. Therefore, after deciding what role expert opinion is to play, the next step is deciding how to collect and assess expert opinion. There is currently no optimal method for this, but the process needs to be made as explicit as possible.

Resource implications and feasibility

In addition to scientific evidence and the opinions of expert clinicians, practice guidelines must often take

into account the resource implications and feasibility of interventions.

Judgments about whether the costs of tests or treatments are reasonable depend on how cost effectiveness is defined and calculated, on the perspective taken (for example, clinicians often view cost implications differently than payers or society at large), and on the resource constraints of the health care system (for example, cash-limited public systems versus private insurance-based systems). Feasibility issues worth considering include the time, skills, staff, and equipment necessary for the provider to carry out the recommendations and the ability of patients and systems of care to implement them.

Grading recommendations

It is common to grade each recommendation in the guideline. Such information provides the user with an indication of the guideline development group's confidence that following the guideline will produce the desired health outcome. "Strength of recommendation" classification schemes (such as the one in the box) range from simple to complex: no one scheme has been shown to be superior. Given the factors that contribute to a recommendation, strong evidence does not always produce a strong recommendation, and the classification should allow for this. The classification is probably best done by the group panel, using a democratic voting process after group discussion of the strength of the evidence.

Reviewing and updating guidelines

Guidelines should receive external review to ensure content validity, clarity, and applicability. External reviewers should cover three areas: people with expertise in clinical content who can review the guideline to verify the completeness of the literature review and ensure clinical sensibility; experts in systematic reviews, guideline development, or both, who can review the method by which the guideline was developed; and potential users of the guideline, who can judge its usefulness.

The guideline can be updated as soon as each piece of relevant new evidence is published, but it is better to specify a date for updating the systematic review that underpins the guideline.

Conclusions

New advances in understanding the science of systematic reviews, the workings of groups of experts, and the relation between guideline development and implementation are all likely in the next 3 to 5 years.

We believe that 3 principles will remain basic to the development of valid and usable guidelines:

- The development of guidelines requires sufficient resources in terms of financial support and people with a wide range of skills, including expert clinicians, health services researchers, and group process leaders;
- A systematic review of the evidence should be at the heart of every guideline; and
- The group assembled to translate the evidence into a guideline should be multidisciplinary.

References

1. Woolf SH. An organized analytic framework for practice guideline development: using the analytic logic as a guide for reviewing evidence, developing recommendations, and explaining the rationale. In: McCormick KA, Moore SR, Siegel RA, eds. *Methodology perspectives.* Washington, DC: US Department of Health and Human Services, Agency for Health Care Policy and Research, 1994:105-13. (AHCPR publication number 95-0009.)
2. Kahan JP, Park RE, Leape LL, Bernstein SJ, Hilborne LH, Parker L, et al. Variations by specialty in physician ratings of the appropriateness and necessity of indications for procedures. *Med Care* 1996; 34:512-23.
3. Coulter I, Adams A, Shekelle P. Impact of varying panel membership on ratings of appropriateness in consensus panels—a comparison of a multi- and single disciplinary panel. *Health Serv Res* 1995; 30; 577-91.
4. Leape LL, Park RE, Kahan JP, Brook RH. Group judgments of appropriateness: the effect of panel composition. *Quality Assur Health Care* 1992; 4:151-9.
5. Kosecoff JH, Kanouse DE, Rogers WH, McCloskey L, Winslow CM, Brook RH. Effects of the National Institutes of Health consensus development program on physician practice. *JAMA* 1987; 258:2708-13.
6. Shekelle PG, Schriger DL. Evaluating the use of the appropriateness method in the Agency for Health Care Policy and Research clinical practice guideline development process. *Health Serv Res* 1996; 31:453-68.
7. Shekelle PG, Kravitz RL, Beart J, Morger M, Wang M, Lee M. Are nonspecific practice guidelines potentially harmful? A randomized comparison of the effect of nonspecific or specific guidelines on physician decision making. *Health Serv Res* (in press).
8. Cochrane Review Handbook. In: Cochrane Collaboration. *Cochrane Library.* Issue 4. Oxford: Update Software, 1998.
9. Dickersin K, Scherer R, Lefebvre C. Identifying relevant studies for systematic reviews. *BMJ* 1994; 309:1286.
10. Gregoire G, Derderian F, Le Lorier J. Selecting the language of the publications included in a meta-analysis: is there a Tower of Babel bias? *J Clin Epidemiol* 1995; 48:159-63.
11. Egger M, Zellweger-Zohner T, Schneider M, Junker C, Lengeler C, Antes G. Language bias in randomised controlled trials published in English and German. *Lancet* 1997; 350:326-9.
12. Schulz KF, Chalmers I, Hayes RJ, Altman DG. Empirical evidence of bias: dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *JAMA* 1995; 273:408-12.
13. Moher D, Jones A, Cook D, Jadad AR, Moher M, Tugwell P, et al. Does quality of reports of randomised trials affect estimates of intervention efficacy reported in meta-analyses? *Lancet* 1998; 352:609-13.
14. Colditz GA, Miller JN, Mosteller F. How study design affects outcomes in comparisons of therapy. I: Medical. *Stat Med* 1989; 8:441-54.
15. Miller JN, Colditz GA, Mosteller F. How study design affects outcomes in comparisons of therapy. II: Surgical. *Stat Med* 1989; 8:455-66.
16. Shekelle P. Assessing the predictive validity of the RAND/UCLA appropriateness method criteria for performing carotid endarterectomy. *Int J Technol Assess Health Care* 1998; 14:707-27.

This paper originally appeared in the *BMJ* 1999; 318:593-6.

COMMENTARY

How to judge practice guidelines

Scott Weingarten, Cedars-Sinai Health System, 200 North Robertson, Suite 205, Beverly Hills, CA 90211; weingarten@csmc.edu

Guidelines are developed to improve clinical decision-making and, ultimately, patient care. Many physicians have become acquainted with at least some guidelines[1]; some may be using guidelines to inform their day-to-day care of patients. An increasing number of studies have demonstrated that guidelines, when effectively implemented, can improve patient care.[2] The quest to make patient care more consistent with the available scientific evidence is likely to continue and will lead to significant discussion about optimal guideline development strategies.

There is an increasing awareness that not all guidelines are created equally; the rigor and amount of resources required to develop and update them varies significantly.[3] There are even published methods to critically appraise practice guidelines.[4,5] The efforts to judge guidelines could guide practitioners and patients to which guidelines are most deserving of their attention and likely to improve patient care.

Importantly, the relative merits of guidelines can be judged from different perspectives. First, guideline developers can debate the attributes of good guidelines and establish criteria to guide the development of future practice guidelines. The recommendations by Shekelle et al in this month's journal, if adopted, would lead to more rigorous and scientifically-based guidelines. Second, users of guidelines (most commonly practitioners) could offer a perspective regarding the attributes of guidelines that make them most useful as they care for patients on a daily basis. Practitioners may value different attributes than guideline developers do. Third, patients may have opinions regarding the attributes of good guidelines. Finally, as more guidelines are developed and tested in clinical practice, there will be information to discern the characteristics of guidelines that are most likely to lead to measurable improvements in care.

For example, the authors recommend that guideline development teams include someone with health services research expertise. Although I am inclined to agree, since I am a health services researcher who assists in the development of guidelines, I cannot support that claim with scientific evidence. No available data show that practitioners value health services research involvement in the development of practice guidelines or that they are more likely to use such guidelines. Available information suggests that practitioners value practical, easy-to-use guidelines that are endorsed by respected subspecialty societies.[1] There are no published data to support that guidelines developed by individuals with experience in health services research are more likely to lead to measurable improvements in patient care than those that are not.

The guideline field may be somewhat analogous to the software and personal computer industry.[6] In the beginning, high-technology innovators and early adopters debated the most desirable features of software and personal computers. As market forces took hold, however, the opinion of the majority of users ultimately determined which personal computers and software programs were successful.

Similarly, it is the beliefs of practitioners that will influence the adoption and rejection of practice guidelines.

Why not recommend that guidelines be developed as methodically and rigorously as possible in all cases? Guideline development consumes scarce health care resources and will ultimately be judged by whether it leads to documented and cost-effective improvements in patient care. Will a guideline developed by a team of experts, using a systematic review of the literature, for $500,000 lead to greater improvements in patient care than a guideline developed by a single expert for $10,000? Those recommending criteria for guideline development must show that each step has value and increases the probability that the guideline will improve patient care. Initially, demonstration of value could come from showing that users of guidelines (practitioners) are more likely to use and trust guidelines developed in accordance with the recommendation. Ultimately, hypotheses regarding the attributes of good guidelines will be validated or rejected through the careful study of the effects of guidelines on patient care.

References

1. Tunis SR, Hayward RS, Wilson MC, Rubin HR, Bass EB, Johnston M, et al. Internists' attitudes about clinical practice guidelines. *Ann Intern Med* 1994; 120:956-63.
2. Grimshaw JM, Russell IT. Effect of clinical guidelines on medical practice: a systematic review of rigorous evaluations. *Lancet* 1993; 342:1317-22.
3. Fang E, Mittman BS, Weingarten S. Use of clinical practice guidelines by managed care physician groups. *Arch Fam Med* 1996; 5:528-31.
4. Hayward RS, Wilson MC, Tunis SR, Bass EB, Guyatt G. Users' guides to the Medical Literature. VIII. How to use clinical practice guidelines. A. Are the recommendations valid? The Evidence-based Medicine Working Group. *JAMA* 1995; 274:570-4.
5. Wilson MC, Hayward RS, Tunis SR, Bass EB, Guyatt G. Users' guides to the Medical Literature. VIII. How to use clinical practice guidelines. B. What are the recommendations and will they help you in caring for your patients? The Evidence-based Medicine Working Group. *JAMA* 1995; 274:1630-2.
6. Moore GA. *Crossing the chasm: marketing and selling high-tech products to mainstream customers.* Harper Business. 1991, New York, New York.

TOPIC IN REVIEW

The primary care of elder mistreatment

Case 1

Mrs. W. is an 85-year-old African American woman followed for hypertension, dementia, and peripheral vascular disease. She lives with her disabled daughter and unemployed son-in-law. Mrs. W. is dropped off at the entrance to the clinic by her chore worker for a scheduled visit with her doctor and is forced to walk 30 yards to the waiting room in her stockinged feet. She is left alone for the interview, during which she appears in pain but denies being mistreated. She tells the doctor, "I'm old and sick, but I won't die in any old age home!" The patient, wearing a soiled dress, is thin and has lost 9 pounds over the past 2 months. Physical examination reveals dry gangrene of the right second and third toes with cellulitis of the right foot. After she adamantly refuses hospitalization, her physician prescribes antibiotics and 100 tablets of acetaminophen with hydrocodone for pain. When the chore worker arrives to pick up the patient, she is hostile toward the clinic staff and claims the patient is faking pain to get attention.

A report is filed with Adult Protective Services (APS), and a home health referral is made to monitor the status of the gangrene and cellulitis. On her second visit, the nurse cannot find the bottle of acetaminophen-hydrocodone tablets. The physician prescribes a fentanyl patch to replace the lost narcotics, but the nurse observes that it is not being changed regularly, although the patient appears in constant pain. After the nurse confronts the daughter and threatens to call APS if Mrs. W.'s care does not improve, the son-in-law fires the home health agency because of the nurse's alleged rudeness and condescension. Four weeks later, Mrs. W. is admitted to the hospital with sepsis, and an emergency above-the-knee amputation of the right leg is performed. She dies a week after being discharged to a skilled nursing facility.

Definitions

Elder mistreatment involves the physical abuse, neglect, psychological abuse, or financial exploitation of an older adult. The lack of standardization in the definitions in the literature has carried over to the statutory definitions used by states to govern reporting and prosecution. Conceptually, physical abuse includes physical acts of violence, such as hitting and slapping, the infliction of injuries, unwanted sexual contact, as well as inappropriate physical or chemical restraint. Neglect refers to the failure of the primary caregiver to meet the care needs of a dependent adult, including the provision of food, adequate hydration, clothing, shelter, personal hygiene, and medical care. Psychological, or emotional, abuse entails actions that are designed to intimidate or inflict emotional harm, such as threats, denigrating statements, or the use of infantalizing language. Isolating and ignoring the elder also fall within the domain of emotional abuse. Financial exploitation involves the misappropriation of an elder's money or property for personal use or gain, whether through embezzlement, fraud, or outright theft. Self-neglect, the inability of an individual to perform essential self-care tasks, is considered by many authorities and states to be a special category of elder mistreatment.

Problems with statistics

Accurate statistics on the incidence and prevalence of elder mistreatment are lacking, in part because victims often are reluctant to reveal abuse out of shame, denial, self-blame, fear of reprisal, or a desire for privacy. The National Elder Abuse Incidence Study, using substantiated Adult Protective Services (APS) reports supplemented with case detection by community "sentinels," estimated a prevalence of 1.3% in 1996 among non-institutionalized persons over age 60.[1] This figure, which includes self-neglect, is far lower than previous estimates. Lachs et al estimated a 6.4% community prevalence of abuse,[2] based on 11 years of referrals of participants in the New Haven epidemiologic cohort to the Connecticut Ombudsman on Aging. Self-neglect was the most

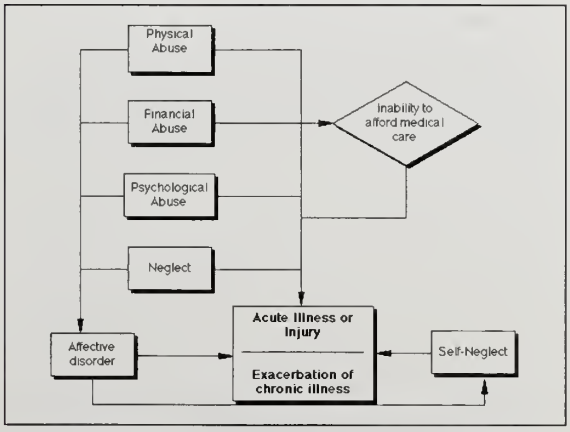


Figure 1 *Paradigm of the health effects of elder mistreatment*

Calvin H Hirsch
Division of General Medicine (Geriatrics)
Department of Internal Medicine

Sara Stratton
Medical Training Center on Family Violence

Roberta Loewy
Section of Bioethics
Department of Internal Medicine

University of California, Davis
Sacramento, CA
95817

Correspondence to:
Calvin Hirsch
chhirsch@ucdavis.edu

commonly reported type (73%), followed by neglect by others (17%). Cross-sectional surveys of elders determined that 3.2% to 4% have experienced some form of abuse (excluding self-neglect) after the age of 65. One-half to 2% of respondents acknowledged physical abuse, while 0.4% reported being neglected.[3,4] Data based on referrals to APS underestimate the true incidence, due to underdetection and underreporting. Surveys suffer from recall bias and the omission of data for the most dependent and cognitively impaired elders. It has been estimated that between 1.1 and 2.5 million older Americans annually experience mistreatment.[5,6]

Ulrike Preuss

Elders are vulnerable

Elder mistreatment as a chronic disease

Abuse, commonly in multiple forms, may occur chronically over months to years,[2,7] sometimes resulting in repeated medical crises.[8] The frequency and intensity of the abuse may escalate over time.[9] All forms of elder mistreatment directly or indirectly affect the health and health care of older patients. The injuries inflicted by physical abuse are the most obvious. Each form of abuse may contribute to anxiety, depression, or post-traumatic stress disorder. Fiduciary abuse may deprive the victim of the financial resources to afford medical services. Neglect may directly cause adverse health outcomes (e.g., dehydration, malnutrition); may lead to harmful delays in seeking medical care; or may lead to noncompliance with a prescribed plan of treatment, contributing to the exacerbation of chronic illness (Figure 1). The consequences of abuse and neglect also include excess hospitalizations and visits to the emergency department (ED). Lachs et al[8] found that 42 of 182 (23%) confirmed elder-abuse victims living in the greater New Haven, Conn, area had at least one visit to the ED attributable to abuse during a 5-year period. Twenty-four percent of their ED visits were injury-related; 22% of these injuries resulted in admission. Over 13 years of follow-up, older victims of elder mistreatment were shown to have a threefold greater risk of dying compared to unabused seniors, after adjustment for age, sociodemographic factors, and comorbidity.[10]

Physician recognition and reporting

The medical consequences of abuse make it likely that the victim will at some point come in contact with a physician. For the dependent elder, the scheduled visit to the primary care physician may be the only opportunity for abuse to be detected. Unfortunately, physicians all too often attribute the medical consequences of abuse to aging or underlying disease. In Michigan, between 1989 and 1993, only 2% of suspected elder-abuse cases were reported by physicians.[11] In a national survey of ED physicians, most doubted or were uncertain of their ability to recognize abuse as well as their state's ability to deal with it effectively once it was reported.[12]

Although all 50 states have adult protective service programs, each state has its own unique laws for reporting elder mistreatment. Health care providers are considered mandated reporters in all 43 states that have mandatory reporting laws. While suspected physical abuse must be reported in these states, the mandate for reporting other types of abuse varies.[13] Effective January 1, 1999, the State of California expanded the mandatory reporting of abuse of an elder to include abandonment, isolation, financial abuse, self-neglect, and neglect by others, in addition to physical abuse.[14] Most states provide reporters with immunity from criminal or civil liability, and the reporting is not deemed a legal breach of patient confidentiality. Failure to comply with mandatory reporting generally is considered a misdemeanor. California law now makes failure to report abuse that results in death or severe injury punishable by a fine of up to $5,000 and/or 1 year in a county jail.[14] It has been argued, from a legal perspective, that a clinician's failure to identify and report cases of obvious abuse and neglect could constitute both negligence and medical malpractice.[15]

Ethical and practical concerns about reporting

Although elder abuse laws are intended to protect vulnerable adults and punish abusers, they may conflict with the principles and practice of medicine, raising doubts among some clinicians about the appropriateness and feasibility of reporting.

VIOLATION OF PATIENT CONFIDENTIALITY

Mandatory reporting potentially violates physician-patient trust and confidentiality and threatens the thera-

peutic alliance between the physician and the caregiver-abuser. A feared consequence is that the patient will change doctors, losing not only continuity of care but also a physician who, by being alert to the situation, might have more success in working with the family to eliminate abuse and achieve the therapeutic goals of the relationship.

VIOLATION OF THE PRINCIPLE, "DO NO HARM"

Once the report is filed, the physician may lose control over the events that follow. Although APS generally subscribe to the principles of freedom over safety, self-determination, and maintenance of the family,[16] the outcome of an APS investigation may be contrary to the patient's desires (e.g., institutionalization).The investigation itself may heighten tension between the victim and abuser, as well as generating resentment of the doctor.

IMBALANCE BETWEEN MANDATE AND PUBLIC FUNDING

The filing of a report does not guarantee either that a satisfactory solution to the abusive situation will be found or that the report will prompt an investigation. For example, the number of staff assigned to APS programs in California declined by 35% between 1990 and 1998. By 1998, fewer than 20% of counties were able to respond to all APS reports, and 45% could not provide longitudinal case management of APS cases.[17] The frustration of not seeing any benefit to the patient after an APS report has been filed is one of the most persuasive arguments against physician reporting.

Despite these concerns, the filing of a report with APS remains the single best way to stop elder mistreatment. Most clinicians do not have the training—or the time—to interview and counsel the victim and alleged abuser, and few can muster the resources offered by most APS. Improperly conducted investigations may harm the chances of stopping the abuse, and place the patient at greater risk. The success of an APS referral depends, in part, on the quality of the information provided and the willingness of the physician to work with APS during the investigation and interventions.

The physician's role in managing elder mistreatment

The primary care of elder mistreatment requires an awareness of its prevalence, risk factors, and clues (Tables 1 and 2). Evaluating a patient's risk for abuse starts with an understanding of the patient's degree of dependence, which is best done through a systematic assessment of the patient's functional and cognitive status. Early research concentrated on the dependency of the elder and caregiver stress as the principal risk factors. Subsequent research has found that the functional dependency of the older adult may be less important than the dependency of the abuser on the elder (e.g., for housing or financial support), especially if the abuser is an adult son or daughter of the elder. Abusers are more likely to have past or present psychiatric problems, a history of alcohol or drug abuse,[9, 18] and underlying personality disorders.[19] Elderly men and women are equally likely to be mistreated.[20] As shown in Table 2, there may be clues to the possibility of elder mistreatment.

Case 2

A 72-year-old woman with moderately severe dementia, uncontrolled diabetes, and uncontrolled hypertension lives with her husband, who is suspected of being an alcoholic. The patient always comes to her appointments with 1 of her 2 daughters, who live nearby, but never with her husband. She is always dishevelled, with evidence of urinary incontinence, and her glycosylated hemoglobin is 12. The daughters claim to visit their mother daily, but consistently have failed to bring in her blood glucose monitoring record so that her insulin can be adjusted. Their reports of the mother's diet indicate that previous dietary counseling has been fruitless. The daughters are reluctant to admit that their father is an alcoholic but acknowledge purchasing liquor for their parents. The physician tells the daughters that because they clearly need more help caring for their mother's medical problems, she will send a referral to a county social worker and public health nurse (i.e., APS) to see if they can come up with a new plan, even though home health already is involved.

Table 1 *Risk factors for elder mistreatment in the community setting. (Adapted from Jones et al*[24])

Excessive dependency of the elder for activities of daily living	
	Resentment by caregiver for giving too much, getting back too little
The stressed-out caregiver	
	Poor premorbid quality of the relationship, external stressors (job, family, finances), lack of social support, emotional burden, depression, increasing care needs of a demented relative
History of family violence (child or spousal abuse)	
Psychopathology in the caregiver	
	Substance abuse, sociopathic personality, financial exploitation of elder
Caregiver dependence on elder	
	Housing, financial support
Sociocultural/environmental	
	Inadequate housing
	Resentment and anger from elder over decline in stature within family
	Demanding personality of elder
	Cultural sanctions against seeking help outside family

Table 2 *Clues for possible elder mistreatment. (Adapted from Kleinschmidt[25] and Lachs & Pillemer.[21])*

General
• Caregiver of cognitively impaired elder absent for appointment
• Failure of caregiver to visit patient in hospital
• Reluctance to answer questions about a suspicious physical finding or illness
• Implausible or vague explanations for injuries given by caregiver or patient
• A history of "doctor hopping"
• Tension or indifference between caregiver and patient
Suspicious physical signs
• Multiple bruises or bruises at different stages of healing
• Bruises in unusual locations
• Pattern injuries (injuries in the shape of the object used to inflict them, such as bite marks, cigarette burns)
• Evidence of old injuries not previously documented or radiographic evidence of old, misaligned fractures
• Broken nose, teeth
• Subtherapeutic levels of drugs
• Patient lacking his or her eyeglasses, dentures, or hearing aid
Caregiver
• Poor knowledge of patient's medical problems
• Excessive concern about costs
• Attempts to dominate medical interview
• Verbal abuse or hostility toward elder or health care provider during encounter
• Evidence of substance abuse or mental health problems
• Evidence of financial dependence on elder
The abused elder
• Fearfulness toward caregiver
• Flinching or reluctance to make eye contact
• Diagnosis of dementia with history of disruptive behavior
• In demented person, unexplained resistance to, or fear of, physical touch, removing clothes, toileting, bathing of private parts
• Depression, anxiety, insomnia

Physician assessment of elder mistreatment

An emphasis on the diagnosis and treatment of the health consequences of mistreatment offers a less threatening approach and may help the physician retain the patient's and suspected abuser's trust while interventions are tried. If abuse is suspected, the patient and caregiver must be interviewed alone in order to elicit uninhibited disclosure and to identify inconsistencies between the two accounts.[21] The clinician should avoid confrontation and blame, while appearing sympathetic to the suspected abuser's perceived burden of caregiving. Table 3 lists examples of questions that may be used to elicit information about mistreatment.

To avoid the surprise and anger that the unexpected visit of an APS social worker might engender, the physician should tell the patient and caregiver that a referral will be made to APS. The law-enforcement implications of APS should be down-played, instead offering APS as an additional service to help the patient's medical problems.

If the patient or caregiver refuses the APS referral, clinicians should explain that they are bound to adhere to state regulations that were developed to help seniors who are not receiving the care they need—for whatever reason. These laws obligate the physician (in the case of mandated reporting) to notify APS.

Keeping the patient safe

The safety of the victim is the paramount consideration, and in certain circumstances, such as escalating physical violence, physicians should immediately contact law enforcement in addition to APS. Hospitalization may be the most expedient way to separate victim and abuser, although the medical necessity may be questioned by third-party payers. In most cases the decision-making capacity of the patient will determine the intervention. If the patient has decision-making capacity but refuses intervention, the patient has the right to remain in the abusive situation. In such cases, the physician should educate

the patient about the medical consequences of abuse and its tendency to increase in frequency and severity. The physician should counsel the patient to develop a safety plan, such as when to call 911 or installing a Lifeline™ emergency alert system. Often the patient who refuses intervention for abuse will accept more frequent monitoring of a specific medical condition. Increased oversight can take the form of more frequent appointments or home health and subspecialty consultations. To avoid biasing the consultant, requests should be framed in terms of a specific medical need. For example, a consultation request to a psychiatrist for evaluation of possible depression secondary to psychological abuse might include the statement, "Please evaluate for depression and, if found, please assess its etiology in light of a possible problematic relationship between Mrs. X and her husband." It is appropriate to mention that an APS referral has been made.

Role of the court

Although a patient may lack decision-making capacity, he or she still is considered legally competent until mental incompetence is determined by the court, which can then impose services. Most states have provisions to arrange guardianship, conservatorship, or financial management, as well as to remove cognitively incapacitated elders from the abusive environment against their will. Usually, forced removal requires a formal psychiatric assessment and the presence of imminent danger to the elder.

Table 4 *Guidelines for reporting to adult protective services*

Urgency of the referral
Likelihood of imminent harm
History
Description of the suspected abuse
The medical/psychiatric consequences of the mistreatment and their acuteness or seriousness.
A list of the patient's chronic illnesses and how they might have been affected.
Predicted impact of the abuse on future health
Likelihood of adverse effect
Anticipated time frame (days, weeks, months)
Pertinent physical findings
If physical abuse, include detailed descriptions of any injuries, using drawings and (if possible) photographs. (Forensic photography may be available in the some emergency departments)
Description of the patient's functional status and care needs
Assessed or estimated decision-making capacity of elder
Suspected abuser's relationship to the patient
Known or suspected risk factors for abuse (e.g., caregiver stress, substance abuse)
Other medical and community services currently being used by patient (e.g., name of home health agency)
When and how best to contact you

Table 3 *Examples of questions to elicit information about mistreatment. (Adapted from Kleinschmidt[25] and Lachs & Pillemer.[21])*

General lead-in questions about the safety of the home environment and who provides help
Do you feel safe where you live?
Who helps you with the things that you have trouble doing yourself?
Who handles your checkbook, pays the bills?
Questions concerning physical abuse
Are you afraid of anyone at home?
Have you ever been slapped, punched, or kicked?
Have you ever been tied down or locked inside in your room or house against your will?
Questions about neglect
Are you made to wait a long time for food or medicine?
Have you been left alone for long periods?
When you need assistance, do you have trouble getting someone to help you?
Questions about psychological abuse
Are you yelled at?
Have you been threatened with punishment or placement in a nursing home?
Are you kept isolated from friends or other relatives?
Do you get the "silent treatment" at home?
Do you have frequent disagreements with your [principal caregiver]?
When you disagree, what happens?

Working with Adult Protective Services

Clinicians should have realistic expectations of their local APS. For example, not all state APS routinely assess the risk of future abuse,[13] and there is great variation between states in the criteria for providing involuntary protective services.[22] Because hospitals with emergency departments or outpatient clinics are required to provide mandatory education about elder mistreatment, they represent a logical mechanism by which APS representatives can inform community physicians about their services. In many communities, APS are unaccustomed to working closely with the primary-care physician. Until such collaboration is routine, physicians should specifically request to be kept informed.

Reporting

The first step in managing suspected mistreatment is to report the case to the appropriate protective services agency. In California, suspected mistreatment occurring in the community is reported to APS or law enforcement (in the case of criminal abuse), while mistreatment in the long-term care setting is reported to the local ombudsman. APS use the report to triage cases, and the content may guide the investigation and prosecution of abuse. Although most primary care clinicians are not accustomed to performing an evidentiary exam, it is important that the documentation be as complete as possible, since physical signs and symptoms recognized by the clinician may resolve before a forensic examiner (if available) can evaluate them. The reporting guidelines in Table 4 will help the clinician provide APS with critical information and promote effective collaboration.

Summary Points

- Elder mistreatment occurs commonly, may be chronic, and can adversely affect the health and health care of the older patient
- Primary care physicians can play a pivotal role in the diagnosis and management of abuse and neglect, by focusing on the medical conditions that they affect or cause
- Nearly all states require physicians to report suspected physical abuse to the local adult protective services program
- Successful management requires effective teamwork between the primary care clinician, APS, consultants, and a variety of community agencies

Working with other services

Although home health may be useful in assessing and managing the medical consequences of mistreatment, drawbacks include a restricted number of visits and, frequently, limited experience in dealing with elder mistreatment. Respite services should be considered in most cases of abuse and neglect. A referral to a chore worker service (a fee-for-service agency or state- or county-funded in-home support service) may alleviate the burden for the caregiver. Chore workers, however, who may receive low wages, minimal benefits, and little oversight, can also abuse vulnerable elders.

Conclusion

For the busy clinician, a geriatrician, usually working with an interdisciplinary team, may be better able to coordinate the time-consuming assessments that are integral to understanding the etiology of the mistreatment and its relationship to the patient's health care needs.[23] The social worker, who is usually part of the geriatric team, can help to maintain effective and essential communication between the primary care physician, consultants, APS, and other involved agencies. Geriatricians are not available in all communities, but in time, the geriatric team may play an integral role in elder-abuse management, in much the same way child protection centers now help pediatricians and child protective services in the area of child abuse.

References

1. National Center on Elder Abuse, Westat Inc. The national elder abuse incidence study: final report. Administration on Aging, United States Government, September 1998. URL: http://www.aoa/gov/abuse/report.
2. Lachs MS, Williams C, O'Brien S, Hurst L, Horwitz R. Older adults. an 11-year longitudinal study of adult protective service use. *Arch Intern Med* 1996; 156:449-53.
3. Pillemer K. Finkelhor D. The prevalence of elder abuse: a random sample survey. *Gerontologist* 1988; 28:51-7.
4. Podnieks E. National survey on abuse of the elderly in Canada. *Journal of Elder Abuse and Neglect* 1992; 4:59-111.
5. Elder abuse and neglect. Council on Scientific Affairs. *JAMA* 1987; 257:966-71.
6. Elder abuse: a national disgrace. Report by the Subcommittee on Health and Long-term Care of the Select Commirtee on Aging: US Congress, Committee Publication 99-502, 1985.
7. Tatara T. Summaries of national elder abuse data: an exploratory study of state statistics. Washingron, D.C.: National Aging Resource Center on Elder Abuse, 1990.
8. Lachs MS, Williams CS, O'Brien S, et al. ED use by older victims of family violence. *Ann Emerg Med* 1997; 30:448-54.
9. Quinn MJ, Tomita SK. *Elder abuse and neglect: causes, diagnosis, and intervention strategies.* New York: Springer Publishing Company, 1997.
10. Lachs MS, Williams CS, O'Brien S, Pillemer KA, Charlson ME. The mortality of elder mistreatment. *JAMA* 1998; 280:428-32.
11. Rosenblatt DE, Cho KH, Durance PW. Reporting mistreatment of older adults: the role of physicians. *J Am Geriatr Soc* 1996; 44:65-70.
12. Jones JS, Veenstra TR, Seamon JP, Krohmer J. Elder mistreatment: national survey of emergency physicians. *Ann Emerg Med* 1997; 30:473-9.
13. Goodrich CS. Results of a national survey of state protective services programs: assessing risk and defining victim outcomes. *Journal of Elder Abuse and Neglect* 1997; 9:69-86.
14. Murray K. Assembly Bill 1780 (Chaptered). Elder abuse: reporting requirements. Sacramento: California State Assembly, September 30, 1998.
15. Moskowitz S. Private enforcement of criminal mandatory reporting laws. *Journal of Elder Abuse and Neglect* 1998; 9:1-22.
16. Anetzberger GJ, Dayton C, McMonagle P. A community dialogue series on ethics and elder abuse: guidelines for decision-making. *Journal of Elder Abuse and Neglect* 1997; 9:33-50.
17. Lockyer W. Senate Bill 2199 (Chaptered). Elder and dependent adult abuse. Sacramento: California State Senate, September 29, 1998.
18. Wolf RS. Major findings from three models projects on elderly abuse. In: Pillemer K, Wolf R, eds. *Elder abuse and neglect: conflict in the family.* Dover, MA: Auburn House Pub. Co., 1986.
19. Anetzberger GJ. *The etiology of elder abuse by adult offspring.* Springfield, IL: Thomas, 1987.
20. Kosberg JI. The abuse of elderly men. *Journal of Elder Abuse and Neglect* 1998; 9:69-88.
21. Lachs MS, Pillemer K. Abuse and neglect of elderly persons. *N Engl J Med* 1995; 332:437-43.
22. Duke J. A national study of involuntary protective services to adult protective services clients. *Journal of Elder Abuse and Neglect* 1997; 9:51-68.
23. Vernon M, Bennert G. 'Elder abuse': the case for greater involvement of geriatricians. *Age Ageing* 1995; 24:177-9.
24. Jones JS, Holstege C, Holstege H. Elder abuse and neglect: understanding the causes and potential risk factors. *Am J Emerg Med* 1997; 15:579-583.
25. Kleinschmidt KC. Elder abuse: a review. *Ann Emerg Med* 1997; 30:463-72.

capsule

Life-threatening licorice. In March 1997, a 44-year-old women walked into the emergency department of a Swedish hospital and promptly had a series of life threatening ventricular tachycardias (*Journal of Internal Medicine* 1999; 245:307-10). Her serum potassium concentration was 2.3 mmol/L After a bewildering variety of investigations—including cardiac ultrasound and endoscopy of her esophagus, duodenum, and colon—she admitted eating 40-70 grams of licorice every day for four months. The metabolic consequences of a surfeit of licorice are well known, but this is the first reported case of a resulting torsades de pointes tachycardia.

capsule

Add exercise to asthma therapy. Exercise training programs in children with asthma are controversial, but two small studies in *Thorax* add to the evidence supporting their use (1999; 45:196-200, 202-6). In the first, individually tailored swimming training improved fitness and reduced exercise induced bronchoconstriction in eight children; in the second, training on an exercise bicycle for two months had a short-term impact on participants' use of medication. One commentator warns, however, that the available evidence is still too weak to justify modifying conventional asthma treatments.

MEDICINE CABINET

Quinolones: which generation for which microbe?

Monica K Lee
Meganne S Kanatani
Department of Pharmaceutical Services
UCLA Medical Center
10833 LeConte Avenue
CHS 16-135
Los Angeles, CA 90095

Correspondence to:
Dr Kanatani
mkanatani@mednet.ucla.edu

Quinolone antimicrobials have been in clinical use since the 1960s. The narrow spectrum of activity and poor tissue and serum concentrations of the early quinolones limited their use to the management of urinary tract infections. Recently, new fluoroquinolones with broader spectrums of activity and improved pharmacokinetic profiles have come to market. Based upon their microbiologic activity against a wide range of pathogens, these agents may be classified into different generations. The differences between these generations can be confusing. This article compares the spectrum of activity as well as the clinical uses among the 4 generations of fluoroquinolones.

Nalidixic acid was the first quinolone antimicrobial released in 1962. Since then, newer fluoroquinolones have been introduced with both an extended spectrum of activity and an improved pharmacokinetic profile. Greater coverage of *Staphylococcus* and *Streptococcus* species, gram-negative organisms including *Pseudomonas aeruginosa,* the atypical organisms, and anaerobes has improved their clinical utility. The pharmacokinetic properties of the newer fluoroquinolones allow for less frequent dosing, thereby improving both clinical efficacy and patient adherence. Additionally, the newer quinolones have fewer adverse effects. Each of the quinolones can be categorized into 1 of 4 different generations based upon their spectrum of activity, similar to the categorization of the cephalosporins (Table 1).

Mechanism of action

Quinolones inhibit DNA synthesis by disrupting DNA gyrase activity (responsible for nicking and introducing negative supercoils to double-stranded DNA prior to its replication).[1] They exhibit bactericidal activity by binding to the DNA-DNA gyrase complex, preventing further DNA synthesis, and demonstrate a concentration-dependent rate of killing (the rate of killing is highest at peak concentrations and declines as the concentration decreases).

Resistance

Fluoroquinolone resistance occurs by 1 of 3 mechanisms or a combination thereof: (1) modifications in the DNA gyrase as a result of spontaneous mutations in chromosomal genes, (2) decreased penetration through the outer membrane of gram-negative rods, and (3) increased intracellular removal of fluoroquinolones by efflux pumps, responsible for the movement of substances (in this case quinolones) from the intracellular to the extracellular environment.[2] If an organism becomes resistant to one of the quinolones, it is usually cross-resistant to other quinolones as well.[1]

First generation

Cinoxacin, nalidixic acid, and oxolinic acid comprise the first-generation group. These early quinolones target gram-negative organisms, including members of the Enterobacteriaceae family (*E. coli, Klebsiella* species, *Proteus* species, etc.), but lack activity against *Pseudomonas aeruginosa,* gram-positive organisms, and anaerobes. Although nalidixic acid was the primary agent used in the past, its poor tissue and serum concentrations now limit its main indication to the management of uncomplicated urinary tract infections. The utility of nalidixic acid is also limited by its relatively short half-life (6 to 7 hours), requiring 4 times daily admininistration,[3] narrow spectrum of activity, and rapid development of bacterial resistance.[1]

Second generation

The addition of a fluorine substituent to the 6-position of the main quinolone ring increased antibacterial activity significantly. Members of the second-generation fluoroquinolones (ciprofloxacin, enoxacin, lomefloxacin, ofloxacin, and norfloxacin) possess enhanced activity against gram-negative bacilli (Enterobacteriaceae and *P. aeruginosa*) with moderate to good activity against *Staphylococcus* species. Tissue penetration of enoxacin, lomefloxacin, and norfloxacin, however, limit their use to the management of uncomplicated urinary tract infections.

Ciprofloxacin and ofloxacin, on the other hand, possess good tissue penetration with excellent intracellular penetration into both macrophages and polymorphonuclear leukocytes. The intracellular levels may be 10-fold higher than serum concentrations, producing enhanced activity against *Legionella pneumophila* (MIC_{90}=0.015-0.06 mcg/ml; the definition of MIC_{90} is the minimum concentration of antimicrobial needed to inhibit growth in 90% of the isolates tested); activity against *Chlamydia pneumoniae* (MIC_{90}=0.5-4μg/ml) and *Mycoplasma pneumoniae* (MIC_{90}=2μg/ml) is variable.[1,4] Ciprofloxacin represents one of the most active fluoroquinolones against *Pseudomonas aeruginosa* (MIC_{90}=0.25-1 μg/ml) and possesses excellent gram-negative activity that is comparable to or superior to that of ofloxacin.[1,4]

In contrast to the broad gram-negative coverage, however, the second-generation quinolones have inferior activity against *Streptococcus pneumoniae* and against both *Enterococcus faecalis* and *Enterococcus faecium.* For this reason, they should not be employed for empiric treatment of community-acquired pneumonia where suspicion for *S. pneumoniae* is high. Both ciprofloxacin and ofloxacin are effective in the management of:

- Complicated/uncomplicated urinary tract infections due to susceptible organisms

Table 1 *Quinolones classified by generation*

Generation	Generic	Brand	Usual Doses	Elimination	AWP Cost / Day
1st	Cinoxacin	Cinobac	500mg PO bid	R>H	$4.89
	Nalidixic acid	NegGram	1 Gm PO qid	R	$8.57
2nd	Ciprofloxacin	Cipro	250-750mg PO bid or 200-400mg IV bid	R (15% H)	$6.82-$7.98 (PO) $28.82-$57.62 (IV)
	Enoxacin	Penetrex	400mg PO bid	R	$6.75
	Lomefloxacin	Maxaquin	400mg PO qd	R	$6.60
	Norfloxacin	Noroxin	400mg PO bid	R	$6.80
	Ofloxacin	Floxin	200-400mg PO/IV bid	R	$7.45-$9.34 (PO) $52.80 (IV)
3rd	Grepafloxacin	Raxar	600mg PO qd	H	$6.18
	Levofloxacin	Levaquin	500mg PO qd	R	$8.05
	Sparfloxacin	Zagam	400mg PO x 1; then 200mg PO qd	R=H	$6.69
4th	Trovafloxacin	Trovan	300mg IV x 1; then 200mg PO/IV qd	H	$7.17 (PO) $36.79-$55.49 (IV)
	Clinafloxacin	investigational	IV/PO; bid dosing	R	-not yet approved-
	Gatifloxacin	investigational	IV/PO; qd dosing	R	-not yet approved-
	Moxifloxacin	investigational	PO; qd dosing	H	-not yet approved-

Dosages: based on usual doses; may vary depending on type of infection, age, renal and hepatic function. Elimination: H=hepatic; R=renal. Cost: based on average wholesale prices (AWP); updated April 1999

- Respiratory tract infections targeting susceptible gram-negative organisms
- Skin and soft tissue infections
- Osteomyelitis (ciprofloxacin only)
- Complicated intra-abdominal infections (ciprofloxacin only; combination therapy)

Third generation

Poor activity against gram-positive organisms led to the development of the third-generation fluoroquinolones: grepafloxacin, levofloxacin, and sparfloxacin. Unlike the older fluoroquinolones, these newer agents have expanded coverage of streptococci and the atypical organisms. Activity against *S. pneumoniae* (including penicillin-resistant strains) and the common atypical organisms (*L. pneumophila, C. pneumoniae, M. pneumoniae*) has improved the clinical utility of fluoroquinolones in the management of community-acquired pneumonia. Recent guidelines published by the Infectious Disease Society of America (IDSA) include the 3rd- and 4th-generation quinolones, doxycycline, or the macrolides among the preferred single-agents for the outpatient management of community-acquired pneumonia; fluoroquinolones are the agents of choice when penicillin-resistant *S. pneumoniae* is suspected.[5] The 3rd-generation fluoroquinolones are highly active against *H. influenzae* and *M. catarrhalis* (range: MIC_{90}=0.015-0.06 µg/ml) but generally are less active against other gram-negative bacteria, especially *P. aeruginosa* (MIC_{90}=1-8 µg/ml vs 0.25-1 µg/ml[ciprofloxacin]), when compared to ciprofloxacin.[3,4]

All 3rd-generation fluoroquinolones are dosed once-daily, due to their relatively long half-lives (range: 8-18 hours).[1,6,7] Dose adjustment for both levofloxacin and sparfloxacin is necessary in renal dysfunction.[8]

Indications for use

- Grepafloxacin and sparfloxacin: community-acquired pneumonia; acute bacterial exacerbation of chronic bronchitis
- Levofloxacin: respiratory tract infections; urinary tract infections; skin/skin structure infections

Fourth generation

The 4th-generation fluoroquinolones (clinafloxacin, gatifloxacin, moxifloxacin, and trovafloxacin) extend the microbiologic activity of the earlier fluoroquinolones with the inclusion of significant anaerobic coverage. Currently, trovafloxacin is the only 4th-generation agent approved for use by the US Food and Drug Administration. It has enhanced in vitro activity over ciprofloxacin against both gram-positive organisms (*S. pneumoniae* MIC_{90}=0.25 vs 4 µg/ml; *S. aureus,* MIC_{90}=0.06 vs 0.5 µg/ml) and anaerobic organisms (*B. fragilis,* [MIC_{90}=0.25 vs 16mcg/ml]; *Prevotella* species, *Peptostreptococcus* species); in vitro activity of trovafloxacin approaches that of metronidazole against susceptible anaerobes (MIC_{90}=0.25-1 µg/ml). Trovafloxacin is generally less active than ciprofloxacin against common gram-negative organisms (Enterobacteriaceae, *P. aeruginosa*).[4,9,10] Its long half-life (12 hours) allows for once daily dosing; dose adjustment is unnecessary in the presence of renal dysfunction due to extensive hepatic metabolism.[6]

Indications for use

- Nosocomial pneumonia (including aspiration pneumonia) when antimicrobial therapy may be streamlined
- Intra-abdominal infections when antimicrobial therapy may be streamlined
- Serious infections associated with penicillin or cephalosporin-resistant *S. pneumoniae*

Adverse effects

Overall, fluoroquinolones are well tolerated with only a 1% to 3% discontinuation rate due to adverse effects.[11] The most common adverse effect reported is gastrointestinal disturbances, including diarrhea, nausea, and vomiting. Phototoxicity is of concern with all quinolones. Sparfloxacin has been associated with the greatest occurrence of phototoxicity (upwards of 8%).[8] The manufacturer recommends avoiding direct and indirect sunlight during and up to 5 days upon completion of sparfloxacin therapy.[8,12] Due to the concern for arthropathy, quinolone use has generally been avoided during pregnancy and in the pediatric population; however, there have been reports of its safety and efficacy in children with cystic fibrosis.[13] Neurotoxicity (mild headache and dizziness) associated with fluoroquinolones has been reported in <1% to 7.4% of patients; seizures (<1% incidence) have been rarely associated with quinolone use.[4,12]

Drug Interactions

One of the most common drug-drug interactions associated with quinolones is chelation reactions resulting in decreased absorption and possible treatment failure. Co-administration of ciprofloxacin with magnesium-aluminum containing antacids has reduced bioavailability by as much as 75% to 91%.[14] Sucralfate, which contains aluminum, reduces the bioavailability of ciprofloxacin by 87.5% to 99%.[14] Concomitant administration of quinolones and potential chelating agents (e.g., aluminum-, magnesium-, calcium-containing antacids, ferrous salts, and zinc) should be avoided or separated by a 2 to 4 hour period.

Decreased clearance of theophylline occurs most commonly with enoxacin and to a lesser extent with ciprofloxacin, grepafloxacin, and norfloxacin. The effect of other newer fluoroquinolones on the clearance of theophylline does not appear to be clinically significant; however, it is important to monitor theophylline levels and toxicities.[4,14] Quinolones can potentiate the elimination half-life of warfarin; monitoring of prothrombin is strongly recommended.[15]

Conclusion

Therapeutic success with the quinolones, expanded indications for use, coupled with the lack of cross-resistance to other classes of antimicrobials, have led to widespread use of these agents.

Increased use, however, has led to the emergence of pathogens resistant to quinolones, particularly among *P. aeruginosa* and methicillin-resistant *S. aureus.* Disturbing trends of increasing ciprofloxacin resistance among *E. coli, Citrobacter freundii,* and *Serratia marcescens* compromise the utility of this antimicrobial class in the future.[16] Based upon these findings, fluoroquinolone use should be reserved for those situations in which drug-resistance is suspected.

Note from the authors: Due to recent postmarketing reports of rare but severe liver injuries, the U.S. Food and Drug Administration issued a Public Health Advisory (6/9/99) to physicians regarding the use of trovafloxacin. This advisory informed physicians that trovafloxacin should be reserved for use in patients meeting all of the following criteria:

- Management of at least one of several FDA-specified infections (see partial listing above, Fourth generation: indications for use) that is judged by the treating physician to be serious and life- or limb-threatening.
- Treatment should be initiated in an in-patient setting (i.e., acute-care hospital or long-term nursing care facility); and
- The treating physician believes that, even given the new safety information, the benefit of the product for the patient outweighs the potential risk.

Furthermore, the duration of therapy should not exceed 14 days and should be discontinued sooner if clinical symptoms of liver dysfunction are present.

References

1. Hendershot EF. Fluoroquinolones. *Infect Dis Clin North Am* 1995; 3:715-29.
2. Stratton CW. Avoiding fluoroquinolone resistance—strategies for primary care practice. *Postgrad Med* 1997; 101:247-55.
3. Owens RC Jr., Ambrose PG, Quintiliani R, Nightingale CH. Classifying quinolone anti-infective agents by generations: a pharmacodynamic approach to rational drug selection. *Issues in Pharmacy* 1997; 3:1-8.
4. Kucers A, Crowe S, Grayson ML, Hoy J. *The use of antibiotics: a clinical review of antibacterial, antifungal and antiviral drugs* (5th Edition) Boston: Butterworth-Heinemann 1997; 965-1176.
5. Bartlett JG, Breiman RF, Mandell LA, File, TM. Guidelines from the Infectious Diseases Society of America. Community-acquired pneumonia in adults: guidelines for management. *Clin Infect Dis* 1998; 26:811-38.
6. Ernst ME, Ernst EJ, Klepser ME: Levofloxacin and trovafloxacin: The next generation of fluoroquinolones? *Am J Health Syst Pharm* 1997; 54:2569-84.
7. Grepafloxacin—a new fluoroquinolone. *Med Lett Drugs Ther* 1998; 40:17-8.
8. Sparfloxacin and levofloxacin. *Med Lett Drugs Ther* 1997; 39:41-3.
9. Bauernfeind A. Comparison of the antibacterial activities of the quinolones BAY 12-8039, gatifloxacin (AM-1155), trovafloxacin, clinafloxacin, levofloxacin and ciprofloxacin. *J Antimicrob Chemother.* 1997; 40:639-51.
10. Wexler HM, Molitoris E, Molitoris D. Finegold SM. In vitro activities of trovafloxacin against 557 strains of anae obic bacteria. *Antimicrob Agents Chemother.* 1996; 40(9):2232-5.
11. Hooper DC: Clinical applications of quinolones. *Biochim Biophys Acta* 1998; 45-61.
12. Lietman PS: Fluoroquinolone toxicities—an update. *Drugs* 1995; 49:159-63.
13. Ramsey BW: Management of pulmonary disease in patients with cystic fibrosis. *N Engl J Med* 1996; 335:179-88.
14. Lomaestro BM, Bailie GR: Absorption interactions with fluoroquinolones—1995 update. *Drug Saf* 1995; 12:314-33.
15. Suh B, Lorber B: Quinolones. *Med Clin North Am* 1995; 79:869-94.
16. Jones RN, Kehrberg EN, Erwin ME. Resistance among important pathogens and the antimicrobial activity of parenteral fluoroquinolones at 43 US medical centers. *Drugs* 1995; 49(suppl 2):179-81.
17. Bryskier A, Chantot Jean-Francios. Classification and structure—activity relationships of fluoroquinolones. *Drugs* 1995; 49(suppl 2):16-28.

CURBSIDE CONSULT

Do growing pains exist?

One in 25 children has recurrent limb pain. Over the past decade we have made considerable advances in our understanding of the likely causes of these recurrent pains. Fifty years ago "growing pains" was a diagnosis in itself, although there was no real understanding of the underlying mechanisms. We then went through a phase of thinking that most limb pain was psychosomatic; this was epitomized by the late John Apley, a down-to-earth and pragmatic pediatrician. He said, "Physical growth is painless, but emotional growth may hurt like hell," and "Growing pains occur in painful families."

There is, of course, more than a grain of truth in each of these observations. We are now in the èra of evidence-based medicine, however, and we can no longer get away with the explanation that these symptoms are caused by the stretching of pain receptors in the epiphyses of long bones as they grow.

A careful history and examination will exclude many of the more serious, and less common, causes of recurrent limb pain, such as recurrent trauma (either accidental or non-accidental), arthritis, muscular disorders, connective tissue diseases, and hematologic problems such as leukemia and neuroblastoma. Most children with growing pains are healthy, and the diagnosis will fit into one of the following categories.

Night cramps

Night cramps classically occur in the posterior calf muscles. The child goes to bed and wakes up complaining of severe pain. Not only will the child usually localize this to the calf muscles, but the muscles themselves may feel "knotted." The child's parents may tell you that the child's calf feels hard and in spasm. Relief is obtained by rubbing the child's calves to alleviate the spasm. The etiology of cramps is unknown, and specific drug treatment is not recommended in children, although it might be in adults.

Hypermobile joints

Many children with so-called growing pains have hypermobility of their joints. The classic story is of a child aged between 3 and 10 who gets pain around the joints. These usually start in the evening after a day of more exercise than usual. The pain may last for 2 to 3 days and is relieved with simple analgesics. The joints most commonly affected are the knees and ankles but elbows, wrists, and occasionally hips may also be painful.

Examination will show joints that are more mobile than normal. There are specific criteria for diagnosing hypermobility syndrome (see below). Any joint that is hypermobile can be subject to aches and pains as a result of overuse. There is often a family history of hypermobility, and children may tell you that they are "double-jointed" or can do contortionist-style tricks, such as sucking a toe or wrapping their legs around their necks. The examination will give the diagnosis, and simple reassurance will relieve much anxiety. Advice on taking analgesics such as acetaminophen when pain is severe and not overindulging in activities that precipitate the pain should suffice. Children certainly should not be excluded from games or other exercise. As a child gets older, the joints become less hypermobile and pain is no longer a problem. Exercise probably speeds this process, so encouraging sensible exercise within the limits of tolerance is to be recommended.

> Physical growth is painless, but emotional growth may hurt like hell.

Key points in the evaluation of growing pains

- Night cramps: localized to calf muscles; spasm felt in muscles
- Hypermobility: pain occurs in the evenings and for 2-3 days after exercise; often a family history of hypermobility; hypermobility shown on examination
- Psychosomatic pains: temporal pattern of pain often found in an unhappy child; look for psychosocial cause

Psychosomatic pains

There is no doubt that children do get psychosomatic pains, and these often manifest in the form of either recurrent abdominal pain or limb pain. The timing of such pain, which often occurs early in the morning on school days but not over weekends or holidays, may offer a clue as to whether it is psychosomatic. There may be clear evidence of problems at school, such as either bullying or an aversion to a particular teacher, or the pain may be a manifestation of stress in another part of the child's life, such as domestic upheaval. It is often worth asking: "If you had a magic fairy who could make any wish come true, what would your three wishes be?" Often the third wish will tell you what the real problem is.

Parents need a cogent explanation of what is causing their child's growing pains. Fortunately, most children with growing pains will fall into one of the three categories that have been described. Anything atypical or persistent must be taken seriously, however. Leukemia and neuroblastoma can present with nonspecific aches and pains. If a child looks ill, he or she should at least have a complete blood count.

Hypermobility scoring system*

Movement	Score
Ability to hyperextend fingers to a position parallel to extensor aspect of forearm	2
Apposition of thumb to flexor aspect of forearm	2
Hyperextension of elbow >10%	2
Hyperextension of knees >10%	2
Ability to put palms flat on floor with knees straight	1

*A score of 6 or more is positive

AW Craft

Department of Child Health, Royal Victoria Infirmary Newcastle upon Tyne NE1 4LP

This paper was originally published in the *Student BMJ* 1998; 6:412-3.

What is a stitch?

Everyone is familiar with the concept of a "stitch." Probably the best description is that the "pain nibbling at his right side suddenly took a pit bull-sized chomp." Obviously, such pain is not life-threatening, but it can be event-threatening. The gradual but inexorable increase in pain can only be relieved by ceasing whatever exercise is being undertaken at the time.

As yet, no scientific appraisal has ever been made of this problem, and a computer search only produced one non-peer reviewed paper on the subject.[1] The main problem with a stitch is its highly variable and random manner of onset. It does seem to be less frequently observed in more highly trained athletes. The manner of onset has produced the hypothesis that the symptoms of a stitch are primarily due to localized muscle ischemia with a shift of blood from the gastrointestinal tract to the exercising muscles—"starved muscle theory." There is no consensus, however, as to whether the intercostal muscles or the diaphragm are being starved.

Some runners believe that a stomach waterlogged from excess hydration can be a factor in developing a stitch.

Matthew Ashton/Empics

An occupational hazard of sprinting

Although there is no specific pattern of lateralization of pain from a stitch, there is an attractive theory that combines the reduction in blood flow to a muscle group with lactic acid overload in these muscles. This may support the theory that improvement in muscle blood flow occurs with increased training and may lead to a reduction in the frequency of having a stitch.

To date, there is no scientific evidence of any link with food intake before exercise and, similarly, many athletes are aware that avoiding dehydration may prevent a stitch. Some runners believe, however, that a stomach waterlogged from excess hydration can be a factor in developing a stitch. Currently, most runners take a moderate amount of fluids before a run and then drink little and often during it.

Unfortunately, there is very little information available. However, adequate fluid intake during running may well be the only solution to this event-threatening problem.

References

1. Sharp D. Side stitch sidestep (avoiding side pains while exercising). *Health* 1990; 4:84.

Gerry Haggerty

Rowallan, 1 Overton Drive
West Kilbride, Ayrshire KA23 9LQ

This article was originally published in the *British Journal of Sports Medicine* 1999; 33:120.

capsule

Ankle sprains pain for months Every day, 23,000 Americans consult a physician because of ankle sprains. One survey suggests that nearly three-quarters continue to have symptoms for months, even years, regardless of the type of treatment they receive (*Archives of Family Medicine* 1999; 8:143-8). Respondents were people with ankle sprains from Minnesota and Wisconsin, 400 of whom were surveyed 6-18 months after injury. Over 40% reported being unable to walk a mile, and a similar percentage could not jump or pivot because of pain or weakness.

TOOLBOX

How to do a sexual physical exam

John Dean; e-mail johndean@netcomuk.co.uk.
Additional editing Etan Milgrom; e-mail Emilgrom@mednet.ucla.edu.

Introduction

Examining a patient or couple with sexual problems involves standard procedures. It can sometimes, however, be fraught with difficulties, often related to psychological and social factors not generally experienced in other situations.

Patients may anticipate the examination with dread and profound embarrassment or, conversely, may see it as a potential source of reassurance and relief. Doctors must be aware of the many popular myths about sex and that their patients may often hold quite idiosyncratic beliefs and fears, which also will need to be addressed.

It is important to explain to patients at the outset how the examination, which is essential in all patients with a suspected physical problem, might help them and to tell them precisely what it entails. An unusual history, odd behavior by either partner during assessment, inconsistent findings on examination, or unexplained bruising or trauma may alert you to an abusive relationship. Any suspicions should not be ignored, but great care and sensitivity are needed to address this issue.

Patient's preferences

Many patients will find examination of the genitalia deeply embarrassing. Success will depend on the cooperation and confidence of your patient, and it is best to defer examination if the patient is uncomfortable and unable to relax.

It is good practice to offer the presence of a chaperone to male and female patients. A substantial minority of patients, both men and women, prefer to be examined by a doctor of their own sex. Remember that patients have made complaints of indecent assault even when their examining doctor was of the same sex.

Cultural differences must also be considered. Many Muslim, Hindu, and Sikh women practice a strict sexual morality. Girls are brought up to be shy and modest, and submitting to a vaginal examination may be abhorred. Remember that our sexual mores are not universally accepted. It is both wise and necessary to explore these issues with the patient before proceeding with an examination.

It is important not to neglect evidence of concomitant disease that may be a contributory factor to the sexual problem. Cardiovascular, respiratory, or neurological diseases may, directly or indirectly, cause sexual problems. Musculoskeletal disorders may lead to sexual problems through chronic pain or immobility. Observe a patient's general mobility, spinal mobility, and movement of the hips and knees. A patient's affect may suggest depression, anxiety, or other mental health problems.

The examination of both men and women should include dipstick analysis of the urine for the presence of glucose. Diabetes is a common cause of erectile dysfunction in men and may also cause autonomic neuropathy affecting sexual response. A measurement of fasting blood sugar concentration would be a more reliable option for detecting diabetes if blood has to be taken for other reasons.

Mary Evans Picture Library

It is important to explain at the outset precisely what an examination entails. (Mercury treatment for venereal disease, circa 1500)

Suggestions for examination

- Remember privacy, warmth, and an unhurried approach are essential
- Consider that one-third of women and one-fifth of men prefer to be examined by a doctor of their own sex
- Carefully consider cultural mores
- Offer patients a chaperone, both for reassurance and for medicolegal reasons
- Assess patients without excluding the possibility that other diseases such as diabetes, hypertension, and depression may have a bearing on their sexual problem

General examination

- Look for evidence of endocrine disease
- Measure blood pressure and perform urinalysis to exclude diabetes
- Check the cardiovascular and central nervous systems
- Examine the abdomen
- Check the external genitalia and, in men, the anus and prostate

Examination of male patients

General

Appearance. Observation of general appearance is important and may reveal signs of androgen deficiency or other endocrine abnormalities. The distribution of facial and body hair and the presence of gynecomastia should be noted. Check blood pressure and radial pulse and palpate the peripheral pulses in men with erectile dysfunction. Evidence of arterial disease, such as the absence of the foot pulses, suggests that an erection problem might be due to arterial insufficiency.

Nervous system. Assess the lumbosacral nervous system if there are indications to do so. There is a dual innervation of the male reproductive system from the sacral roots

(S2-4) through the pudendal and pelvic nerves with predominantly somatic and parasympathetic fibers, and from the thoracolumbar roots (T11-L2) through the hypogastric, sympathetic, and pelvic nerves. Tactile (dorsal column) and pinprick (spinothalamic tract) sensation in the perineal and lower limb dermatomes should be assessed. The condition of the perineal reflexes may provide evidence of spinal cord dysfunction.

Abdomen. Check for abdominal surgery or intra-abdominal pathology such as a palpable bladder or kidneys. Hernias may also cause pain and sexual problems.

Investigations for male sexual dysfunction

In erectile dysfunction

- Urine analysis for glucose or a blood sugar test to exclude diabetes

In loss of sex drive

- Testosterone (9:00 AM sample)
- Sex hormone binding globulin (SHGP)
- Free androgens (calculated from the above)
- Luteinizing hormone (LH)
- Prolactin
- Luteinizing hormone and testosterone have a negative feedback relation similar to that of thyroid-stimulating hormone and thyroxine. This can be useful in distinguishing hypogonadism and pituitary disorders as causes of testosterone deficiency.
- Prostate-specific antigen and other investigations are necessary only when coexisting disease is suspected

National Medical Slide Bank

Presence of gynecomastia should be noted. This usually settles spontaneously but, rarely, may be severe enough to warrant breast reduction

Rectal examination

- Look for anal warts, hemorrhoids, sinus, or fissure

The prostate

- Should be smooth and symmetrical with the firmness of a tensed thenar eminence
- May be tender but should not be painful
- Hardness, irregularity, or asymmetry suggests malignancy and needs urgent referral

Genital

The appearance of the external genitalia and any apparent developmental anomalies should be noted.

Penis. The size of the flaccid penis is variable, but is usually 5-10 cm in length. It may seem smaller in obese men, being buried in the pubic fat. The presence of any firm plaques of Peyronie's disease should be assessed. The foreskin, if present, should be retracted, and any pain, restriction, or scarring noted. The position of the urethral orifice should be confirmed, and the presence of genital warts or other infective problems noted.

Testes. The testes should feel smooth and symmetrical. The epididymes can be palpated and, again, should be symmetrical and uniform. The vasa should be palpable as firm cords without swellings. A varicocele can sometimes be felt as a swelling above the testicle, more commonly on the left side, and is often seen better in the standing position. They are often cited as a cause of fertility problems or pain, but the evidence is inconclusive.

Prostate gland. A rectal examination should be performed (and any perianal problems noted) to assess the size and shape of the prostate. The size of the gland can vary, but it should be firm, smooth, and symmetrical with a uniform consistency (the same firmness as the thenar eminence when the tips of the thumb and forefinger are pressed together), and the median groove should be palpable. It should not be tender to gentle pressure. If it feels hard, irregular, or asymmetrical, this suggests prostatic malignancy. Tenderness often indicates prostatitis, which can be a cause of perineal pain or pain on ejaculation. In either case, further investigation is warranted, and referral to a urological or genitourinary medicine specialist should be considered.

Testing of reflexes

Perianal reflexes
The muscular contractions provoked in these reflexes can usually be seen or palpated

Bulbocavernosus reflex (S2 and S3)
Firmly squeezing the glans penis provokes a contraction of the bulbocavernosus muscle located between the scrotum and anal sphincter

Bulbo-anal reflex (S3 and S4)
Firmly squeezing the glans penis provokes a contraction of the anal sphincter

Anal reflex (S4 and S5)
Stroking or scratching the skin adjacent to the anus provokes a contraction of the anal sphincter

Examination of female patients

General

As in the male patient, observation of general appearance is important. Assess the development of secondary sex characteristics and exclude hirsutism and other signs of virilization. Check the blood pressure, radial pulse, and urine. Examine the abdomen and the reflexes including a check of the anal reflex if a neurological problem is suspected.

Examining a female patient

- Examination is necessary only when a physical problem is suspected
- Note the general appearance
- Check secondary sexual characteristics as well as pulse, blood pressure, and urine
- Examine cardiovascular system, central nervous system, abdomen, and external genitalia
- To assess stress incontinence, examine the patient with a full bladder and ask her to cough
- Digital and speculum examination of the vagina should be carefully made
- Rectal examination is rarely necessary

Investigations for female sexual dysfunction

- Endocrine investigation has limited role but is necessary in women with menstrual irregularity or other symptoms of estrogen deficiency
- Follicular-stimulating hormone and luteinizing hormone
- Estradiol
- Prolactin to exclude a pituitary prolactinoma
- Thyroxine, as in men; hyperthyroidism and hypothyroidism can cause dysfunction in sexual drive and arousal
- Other investigations only when coexisting disease is suspected

Genital

Inspect the external genitalia for any apparent developmental anomalies. Note the condition of the labia minora, clitoris, urethral orifice, vagina, and anus and whether there is evidence of warts or other infections. Is the vulval skin healthy or is there evidence of atrophy and estrogen deficiency? Are hymenal remnants or adhesions present? Note evidence of previous childbirth and scarring from perinatal tears or an episiotomy.

Urinary incontinence can cause a problem with sexual activity, so it is important to examine the patient with a full bladder. Both stress incontinence and detrusor instability may be the culprit; the latter sometimes is associated with voiding at orgasm. With the patient in the left lateral position, ask her to cough vigorously while you observe the urethral orifice: a jet of urine suggests stress incontinence. If incontinence is a substantial problem, referral for urodynamic assessment by a urologist or gynecologist is prudent.

Speculum examination should be performed, and any pain or vaginal discharge during the procedure should be noted. The appearance of the vagina and cervix should be assessed, and, if appropriate, bacterial and chlamydial swabs may be taken from the vagina and endocervical canal. Excluding chlamydiosis is especially important in women with dyspareunia.

Gentle digital examination of the vagina helps in identifying tenderness and muscle spasm. If tolerated, a bimanual examination should be performed to assess the condition of the cervix, uterus, and adnexa. Particularly note any tenderness, thickening, or swellings, which often require referral for further assessment by a gynecologist. The position of the uterus, either anteverted or retroverted, can be noted, but this is rarely a cause of sexual problems. Beware of commenting on the position of the uterus to your patient unless you are prepared to address the matter fully.

Rectal examination in a woman is rarely necessary unless an anal or rectal problem is suspected. However, do look at the perianal skin for evidence of scarring, warts, or infection.

Conclusion

When the examination of the patient has been concluded, it is important to give him or her as clear an explanation of the findings as is possible. The findings are often entirely normal, and this reassurance can be very important as a first step in a patient's recovery of his or her sexual well-being.

John Dean is general practitioner and runs a sexual dysfunction clinic in Plymouth, U.K. Etan Milgrom is associate clinical professor of family medicine and associate predoctoral director of family medicine at UCLA School of Medicine.

This article is adapted from the *ABC of sexual health*, edited by John Tomlinson, physician at the Men's Health Clinic, Winchester and London Bridge Hospital.
© British Medical Journal 1998.

This article was originally published in *BMJ* 1998; 317:1641-1643.

PRACTICE POINT

What drives patients to hum

Hummingbirds need a lot of food in the evening. Then they roost and drop their body temperature. This bed-time calorie load and reduced metabolic rate enables them to survive the night.

We had just moved a few blocks across a suburb in the north of San Diego. Some young relatives of my German wife visited almost immediately a new house that was in chaos. An afternoon project was to obtain and install a new hummingbird feeder (I could not bear to harm the birds by removing the old feeder from our previous house, which was still unsold).

Hummingbird feeder technology is rather simple: a red apparatus with a yellow center attracts the birds. A glass reservoir of 33% solution of granulated sugar provides the calories (running short of white sugar a few months before, I had learned that brown sugar is of no interest to hummingbirds). To the delight of our young guests, within five minutes of feeder installation, the first hummingbird arrived. Within two hours, five of them were competing for this new food source hanging under the eve of our house.

Usually, hummingbirds are extremely territorial. A dominant male will vigorously defend, for hours on end, an artificial feeder, or even a single Fuschia plant. To my surprise, the dominant hummingbird at this new house had an entirely different strategy to he who was King of the feeder at the old place. This new chap sat on top of the feeder, thus being dubbed "Snoopy" by our young German guests, and drove off any competitor who attempted to feed three inches below. The Boss at the old house perched and chirped in a nearby tree, and attacked his competitors at a high speed developed by diving from his sentinel position.

And then it happened. Just after sunset, the belligerent Snoopy permitted no fewer than five other hummingbirds to share the four feeding apertures. In a moment, the ingrained, reproducible behavior of a unique hummingbird had changed into exactly the opposite.

Sometimes we are surprised by the choices that our patients make. People often request treatments that their doctors think are suboptimal. People who cannot afford yet another baby still fail to take precautions that they understand well. Some patients inexplicably withdraw half-way through a clinical trial. Well-informed patients often take decisions that are not evidence-based.

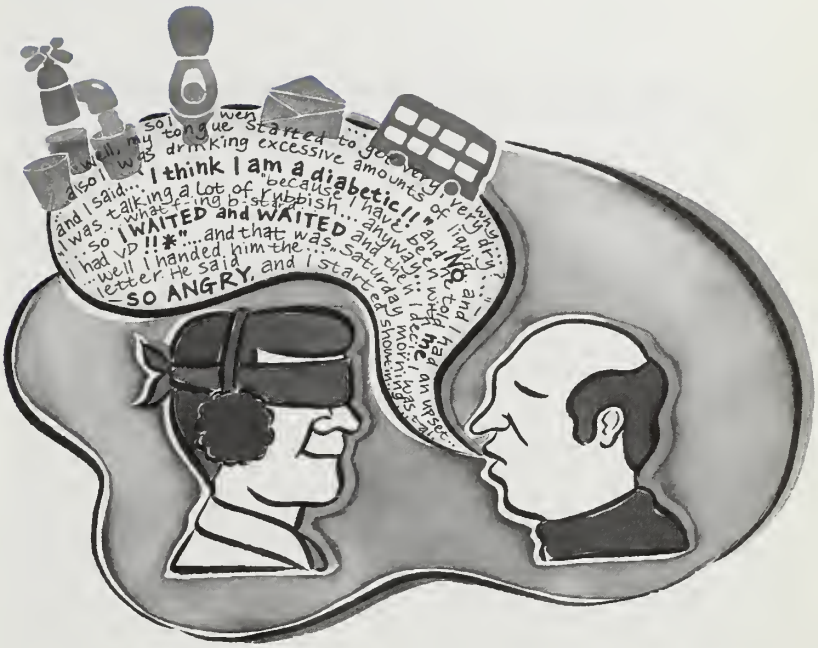
For some good reason, Snoopy, an identifiable individual hummingbird, suddenly reversed his ingrained, biologically predicated behavior. Surely our patients deserve the same opportunity at a moment's notice, even if they mystify us.

Tony Fox, Rancho La Costa, CA

Culture and Medicine

Why study narrative?

One day when Pooh Bear had nothing else to do, he thought he would do something, so he went round to Piglet's house to see what Piglet was doing. It was snowing as he stumped over the white forest track, and he expected to find Piglet warming his toes in front of the fire, but to his surprise he saw that the door was open, and the more he looked inside the more Piglet wasn't there.[1]



What is narrative?

The above excerpt from the opening chapter of a well-known children's story illustrates a number of features of narrative as a linguistic form. First, it has a finite and longitudinal time sequence: it has a beginning, a series of unfolding events, and (we anticipate) an ending. Second, it presupposes both a narrator and a listener whose different viewpoints affect how the story is told. Third, the narrative is concerned with individuals; rather than simply reporting what they do or what is done to them, it concerns how those individuals feel and how people feel about them. Both Pooh Bear, trudging hopefully through the snow, and Piglet, mysteriously absent from his usual place beside the fire, are already characters in the story rather than merely objects in the tale.

The narrative also provides information that does not pertain simply or directly to the unfolding events. The same sequence of events told by another person to another audience might be presented differently without being any less "true." This is an important point. In contrast to a list of measurements or a description of the outcome of an experiment, there is no self-evident definition of what is relevant or what is irrelevant in a particular narrative. The choice of what to tell and what to omit lies entirely with the narrator and can be modified at his or her discretion by the questions of the listener.

Finally, the narrative is absorbing. It engages the listener and invites an interpretation. It offers us the experience of "living through, not simply [knowing] about" the characters in the story.[2]

Summary points

- The processes of getting ill, being ill, getting better (or getting worse), and coping (or failing to cope) with illness can be thought of as enacted narratives within the wider narratives (stories) of people's lives
- Narratives of illness provide a framework for approaching a patient's problems holistically and may uncover diagnostic and therapeutic options
- Taking a history is an interpretive act; interpretation (the discernment of meaning) is central to the analysis of narratives (for example, in literary criticism)
- Narratives offer a method for addressing existential qualities such as the inner hurt, despair, hope, grief, and moral pain that frequently accompany, and may even constitute, people's illnesses
- The lost tradition of narrative should be revived in the teaching and practice of medicine

Narratives in the experience of illness and healing

We "dream in narrative, daydream in narrative, remember, anticipate, hope, despair, believe, doubt, plan, revise, criticize, construct, gossip, learn, hate and love by narrative."[3] Episodes of sickness are important milestones in the enacted narratives of patients' lives. Thus, not only do we live by narrative, but often with our doctor or nurse as a witness,[4] we fall ill, get better, get worse, stay the same, and finally die by narrative, too.

The narrative provides meaning, context, and perspective for the patient's predicament. It defines how, why, and in what way he or she is ill. The study of narrative offers a possibility of developing an understanding that cannot be arrived at by any other means. Doctors and therapists frequently see their roles in terms of facilitating "alternative stories that make sense from the patient's point of view."[5, 6] It has been argued that in psychotherapy the role of the therapist goes further: the therapist should assist the patient in his or her attempt to construct and work through the unconscious elements of a half-written personal story.[7]

Understanding the narrative context of illness provides a framework for approaching a patient's problems holistically, as well as revealing diagnostic and therapeutic

Trisha Greenhalgh
Department of Primary Care
Imperial College School of Medicine at St Mary's
London W2 1PG
United Kingdom

Brian Hurwitz
Department of Primary Care and Population Sciences
Royal Free and University College London Medical School
London N19 5NF
United Kingdom

Correspondence to:
Dr Greenhalgh
p.greenhalgh@ucl.ac.uk

Robert's story

Doctor: Tell me how you first found out that you were diabetic.

Patient: Well my tongue started to get very, very dry and also I was drinking excessive amounts of liquid, and also I had an upset stomach. So I went to my doctor and told him all this, and all he told me was that I had an "upset stomach." And I told him then that I think I am a diabetic, and he told me that I was talking a load of rubbish.

Doctor: Why did your symptoms suggest diabetes to you?

Patient: Because I have been with a diabetic before who has now died. I had known him since he was 9 years old, so the symptoms I had, he [had] described to me before. And that is how I knew I thought I was a diabetic. So I went to another doctor and he told me the same thing: that I had an upset stomach. So I waited and waited and waited. Then I decided to go back to my doctor, when my urine was starting to crystallize, and he told me that I had VD.

Doctor: What do you mean?

Patient: When I was urinating, the end of my penis started getting all white and also sometimes when the urine hit the pan it was starting to go clear white.

Doctor: What happened next?

Patient: Well, I decided to go down to the VD clinic…and I went in there on Friday night and I handed him the letter. And he read it and he said to me, "What do you think you [have]?" And I said, "I think I [have] diabetes." And he said, "What [idiot] sent you here? He should have seen this before you were sent here." So he said to me, "Look, I cannot do anything for you tonight, but please report to the hospital the next morning." (That was Saturday morning.) So I went back home and I came down [on] Saturday morning, but with me walking down on Friday night and [on] Saturday morning, what normally takes me about 5 minutes, took me 35 minutes just to reach the bus stop.

Doctor: Why was that?

Patient: Because I was so weak I could hardly move at all. So I went down, got down to [the hospital], went in and told the [nurse] at reception that I would like to see somebody from the diabetes clinic. And she read the letter. Then she told me that I could not get an appointment [for two weeks]. At this stage I was really very angry, and I started shouting at her. As that started, a nurse came out from [the emergency room] and she read the letter. As soon as she read the letter she shouted to a nurse to get a wheelchair, she dumped me in the wheelchair, and took me straight upstairs to the diabetes clinic.

options. Furthermore, narratives of illness provide a medium for the education of both patients and health professionals and may also expand and enrich the research agenda. Indeed, it is thought that anecdotes, or "illness scripts," may be the underlying form in which we accumulate our medical knowledge.[8, 9] Medical students rely on anecdotes of extreme and atypical cases to develop the essential ability to question expectations, interrupt stereotyped thought patterns, and adjust to new developments as a case unfolds.[10]

The dialogue to the right took place between one of us (BH) and a patient seen in a diabetes clinic. The conversation was recorded on tape and is reproduced almost verbatim with the patient's consent. There are a number of important points in the story. First, there is the immediacy of the patient's voice; his particular way of explaining things cannot be ignored by a listener or reader, although this would be impossible to capture were the story to be retold in the standard forms used for medical histories. Second, the onset of this man's disease is inextricably embedded in a narrative structure within which he recounts with almost choreographic precision how the symptoms unfolded and his efforts to communicate them.

Despite the passing of 30 years, the patient's utter helplessness at the hands of his medical attendants is chilling. It is not simply that his doctor did not seem to listen to him: the doctor's advice and inaction were predicated on an entirely different story from one that required urgent intervention. Asher was graphic in drawing attention to the dangerous tendency of clinicians to see the expected and unconsciously dismiss the anomalous: "We have to beware of this suppressive faculty which, by producing selective deafness, selective blindness and other sense rejections, can so easily suppress the significant and the relevant."[11, 12]

The study of meaning

Even the most pompous professors have been known to warn their students, "Listen to the patient: he or she is telling you the diagnosis." A more sophisticated view holds that when doctors take a medical history they inevitably act as ethnographers, historians, and biographers, required to understand aspects of personhood, personality, social and psychological functioning, and biological and physical phenomena.[13]

The notion of interpretation (the discernment of meaning) is a central concern of philosophers and linguists, but it is a concept with which doctors and other scientists are often unfamiliar, and hence uncomfortable. Hunter, a professor of literature with a strong involvement in medical education, writes somewhat controversially that clinical medicine "shares its methods of knowing with history, law, economics, anthropology,

and other human sciences less certain and more concerned with meaning than the physical sciences. But unlike those disciplines, it does not explicitly recognize its interpretive character or the rules it uses to negotiate meaning."[10] She is puzzled by the medical profession's preoccupation with the gold standard of science in clinical practice and believes that medicine is better characterized as a "moral knowing, a narrative, interpretive, practical reasoning."[14, 15]

A lost tradition

The oral tradition of myths and legends, which are continually recreated by word-of-mouth in successive generations, still features prominently in many non-Western societies and impacts profoundly on the experience of health and illness in these societies.[16] Perhaps it is partly because Western culture has lost its grip on this oral tradition that the skills of listening to, appreciating, and interpreting patients' stories are only rarely upheld as core clinical skills in medical curriculums. Much of the current emphasis in medical training is on the student's acquiring the ability to express a patient's problem in the structured and standardized format that has come to be known as the "medical history" in the United Kingdom and "clinical clerking" in North America. It has been shown that somewhere between the first year and the final year of medical education, students exchange a native facility for eliciting and appreciating patients' narratives for the learned expertise of constructing a medical history.[17]

Narratives frequently appear in a vestigial form in the conventional clinical encounter of modern times. Certain descriptions of symptoms appear to be fragments torn from elaborate stories. These are alighted on by clinicians as especially revelatory: "My shortness of breath always gets worse when I lie down, but the funny thing is the pain only comes on when I climb stairs" or "I was washing the dishes when everything went black: it was like a curtain coming down." Less familiar experiences may be just as important to the patient but the value of such "classic" symptoms to doctors as readers-of-signs is akin to a mirror held up to nature: so closely are they aligned to physiological and pathological mechanisms that the story fragments faithfully portray, in linguistic form, particular biological dysfunctions.

At its most arid, modern medicine lacks a measure of existential qualities such as the inner hurt, despair, hope, grief and moral pain that frequently accompany, and often indeed constitute, the illnesses from which people suffer.[18] The relentless substitution during the course of medical training of skills deemed "scientific"—those that are eminently measurable but unavoidably reductionist—for those that are fundamentally linguistic, empathic, and interpretive should be seen as anything but a successful feature of the modern curriculum.

The core clinical skills of listening, questioning, delineating, marshaling, explaining, and interpreting may provide a way of mediating between the very different worlds of patients and health professionals. Whether these tasks are performed well or badly is likely to have as much influence on the outcome of the illness from the patient's point of view as the more scientific and technical aspects of diagnosis or treatment.[18]

Why study narrative?

In the diagnostic encounter, narratives:
- Are the phenomenal form in which patients experience ill health
- Encourage empathy and promote understanding between clinician and patient
- Allow for the construction of meaning
- May supply useful analytical clues and categories

In the therapeutic process, narratives:
- Encourage a holistic approach to management
- Are intrinsically therapeutic or palliative
- May suggest or precipitate additional therapeutic options

In the education of patients and health professionals, narratives:
- Are often memorable
- Are grounded in experience
- Encourage reflection

In research, narratives:
- Help to set a patient-centered agenda
- May challenge received wisdom
- May generate new hypotheses

This paper was originally published in the *BMJ* 1999; 318:48-50.

References

1. Milne AA. *The house at Pooh corner.* London: Methuen, 1974.
2. Anderson C. Literature and medicine: why should the physician read...or write? In: Peterfreund S, ed. *Literature and science.* Boston, MA: Northeastern University Press, 1990. (Quoting LM Rosenblatt.)
3. Widdershoven G. The story of life: hermeneutic perspectives on the relationship between narrative and life history. In: Josselson R, Lieblich A, eds. *The narrative study of lives.* London: Sage Publications, 1993. (Quoting B Hardy.)
4. Berger J, Mohr J. *A fortunate man: the story of a country doctor.* Harmondsworth: Penguin, 1967.
5. Launer J, Lindsey C. Training for systemic general practice: a new approach from the Tavistock Clinic. *Br J Gen Pract* 1997; 47:453-6.
6. Brody H. My story is broken: can you help me fix it? *Lit Med* 1994; 13:91-4.
7. Holmes J. Narrative in psychotherapy. In: Greenhalgh T, Hurwitz B, eds. *Narrative based medicine: dialogue and discourse in clinical practice.* London: BMJ Books, 1998:176-84.
8. Schmidt HG, Norman GR, Boshuizen HPA. A cognitive perspective on medical expertise: theory and implications. *Acad Med* 1990; 65:611-21.
9. Custers EJ, Boshuizen HP, Schmidt HG. The influence of medical expertise, case typicality, and illness script component on case processing and disease probability estimates. *Memory and Cognition* 1996; 24:384-99.
10. Hunter K. "Don't think zebras": uncertainty, interpretation, and the place of paradox in clinical education. *Theor Med* 1996; 17:225-41.
11. Asher R. Clinical sense: the 1959 Lettsonian lectures. In: Avery Jones F, Richard Asher, eds. *Talking sense.* London: Pitman Books, 1972:3.
12. Epstein J. *Altered conditions: disease, medicine and storytelling.* New York: Routledge, 1995.
13. Hunter KM. Narrative, literature, and clinical exercise of practical reason. *J Med Philos* 1996; 21:303-20.
14. Hunter KM. *Doctors' stories: the narrative structure of medical knowledge.* Princeton, NJ: Princeton University Press, 1991:12.
15. Ratzan RM. Winged words and chief complaints: medical case histories and the Parry-Lord oral-formulaic tradition. *Lit Med* 1992; 11:94-114.
16. Preven DW, Kachur EK, Kupfer RB, Walters JA. Interviewing skills of first year medical students. *J Med Education* 1986; 61:842-4.
17. Kleinman A. *The illness narratives.* New York: Basic Books, 1988.
18. Balint M. *The doctor, his patient and the illness.* London: Tavistock Publications, 1957.

WJM interview with Dr. James Orbinski

Miriam Shuchman

As a medical student at McMaster University in Canada, James Orbinski was intent on a research career. He spent a year in Africa, doing what he describes as "very technical and very advanced research on pediatric AIDS." While there, he had a moment of epiphany. Health, he realized, was far more than a technical concern.

Surrounded by the growing tensions in the small African nation of Rwanda—tensions which would erupt into full-scale genocide several years later—Orbinski came to believe that the social and political dimensions of health were more important to people's wellbeing than the technical study he was involved in. He left research and went to work for Medicins sans frontières/Doctors without borders (MSF), a worldwide organization that provides urgent medical relief in areas of the world beset by war and other human catastrophes.

Within a few years, Dr. Orbinski had graduated from medical school and was back in Africa as MSF's medical coordinator for refugees fleeing the famine in Somalia. MSF's doctors participated in a massive relief effort aimed at restoring famine victims to health. In 1994, Dr. Orbinski returned to Rwanda to be MSF's chief of mission during the genocidal wars there.

Last year the 38-year-old doctor was elected president of MSF. I spoke with him recently about MSF's ongoing work in the former Yugoslavia, the latest region of the world to be torn apart by war and genocide.

Miriam Shuchman
Co-editor, *WJM*

MS: What is MSF doing now in the Kosovo region?
JO: At this point, MSF is providing emergency medical services to the refugees at border stations and in several of the camps in the border regions. In many cases, people have been forced from their homes. Some have seen individual family members beaten, raped or murdered. Some have watched their homes robbed and destroyed. They've been forced to leave either by car or on foot, journeying through the mountains over a 3- or 4-day period before they reach the border. The direct medical consequences of that are all the risks of a long journey that people were unprepared for.

MS: What illnesses are seen at the border stations?
JO: At the borders what we're seeing is that when people come across, particularly the elderly, they are physically exhausted and in many cases people literally collapse as they cross the border. The other major problem that we see is profound psychological trauma. People have a very deep need to tell their stories, to describe the atrocities they've witnessed and experienced.

Then there are the minor cuts and bruises and lacerations, because in many cases people have walked over hills and mountains and been out in the open air for three or four days, often carrying young children or carting their old folks, so they're suffering from exposure. There's a relatively high incidence of acute respiratory tract infections.

MS: What medical services can you provide at the border, apart from bandaging bruises?
JO: People are rehydrated. They're given a place to rest. Sometimes they're given mild sedatives.

The other major problem we're focusing on is epidemic prevention and management. Refugees in this sort of situation are highly susceptible to infectious diseases because of the population being concentrated, and with poor water and poor sanitation the risk of infectious disease increases. We've seen a number of cases of measles in Albania at the border crossings. Measles is potentially a deadly epidemic for children, so we've been working with the World Health Organization to develop a vaccination program.

In a nutshell, what we're doing is providing emergency medical services at the border and in various refugee collection sites throughout the area, and we're doing basic epidemiologic monitoring, since that's how you prevent epidemics from happening.

We also have a mental health program at the border regions, where people can stay for 3, 4 or 5 days at the border. They've been traumatized. They're offered counseling and they're assessed.

Map of the Kosovo region

Another thing we've been doing is to provide necessary supplies to people. The largest number of refugees are accommodated in people's homes. These are poor people and they lack very basic things: soap, toilet paper, toothbrushes, diapers, hygiene items. We've also focused on the major humanitarian issue in the region, which is to ensure the safety of people who remain in Kosovo, and to ensure the protection of people's rights as refugees. They have the right to asylum, the right not to be forcibly deported.

MS: You mentioned preventing epidemics. Concretely, how do you do that?

JO: It's really important to visualize what's actually happening on the ground. There are 100s of 1000s of people who arrive into an area where the services required for them do not exist. People are sleeping in fields, on street corners, with little access to clean water. The figure we use is that minimum water consumption per person per day is 5 to 7 liters. That's for drinking and cooking and washing. If you think about what that means, a liter of water is quite valuable. Access to safe, clean drinking water is a primary issue for us to deal with.

The second thing is defecation. No matter where you are, it's a normal human bodily function. If there aren't proper toileting services, then people will have to toilet wherever they are. So in that sort of circumstance we designate defecation zones. Then we set up the clean water zone at a site far away from the defecation zones so that there's a space, a filter, between the two.

MS: What is a defecation zone or a clean water zone? What does it look like?

JO: Either we bring in portable latrines or we dig pit latrines. Then we build very rudimentary structures where people can clean themselves and bathe. We have a very specialized pumping system and portable tanks and portable water systems that we fly in. We can set that stuff up in a matter of hours, maybe 6 hours or so. Once it's set up, you designate people for keeping the tanks and the pumping system properly maintained. In the southern part of Albania, we've tapped into the public water system and set up piping from the central system. In other cases we'll actually drill for water and then set up pumping and a containment system.

The first two priorities in epidemic prevention are adequate, safe, clean drinking water and control of human sanitation. The third priority is disease surveillance: setting up a very simple disease monitoring system where you can detect potentially epidemic or potentially deadly diseases very quickly and respond very quickly. This means detecting acute diarrhea, measles, meningitis, dysentery. At a very practical level what it means is setting up health treatment posts were people can go. You set up a tent in the

Medecins Sans Frontières provides medical relief in a refugee camp

fields where there are 1000s of people, a health tent where people can go to get treated or to take a sick child, and you simply record on a daily basis a tally of the incidence of certain diseases. Then you centralize this and try to analyze it within a few hours. You encourage community leaders to make sure people go for treatment or report certain signs and symptoms. It's very, very rudimentary, but it's actually the basis for any public health program.

MS: The images we've been seeing on television may be different from what you've seen as a physician. Can you describe the images that you bring away from your recent travels through the refugee areas?

JO: I spent time in two cities in Southern Albania, Krukec and Krume. The images that come to mind are of the people staying in the mosques in those cities. There's a mosque in each city and there are 100s of people sleeping in and around the mosques. They make small fires and try to cook their food there. The most striking feature to me is that the families are very strong and they have stayed together in large, extended family groups. They have nothing, they've lost everything. I think what strikes me the most is the incredible dignity of the Kosovo Albanians and their ability to maintain cohesion and families.

Around every fire you'll see a baby being swung gently in a hammock. The hammock is created by two people

holding either end of a twisted sheet or blanket, and they're rocking this baby calmly, just as if they were at home.

MS: What are your long-range concerns for MSF's work in the Kosovo area?
JO: We can medicalize what is essentially a political crisis, and we have to be careful we don't do that. People come across the border and they have nightmares, tremors, tachycardia. You can focus on the syndrome—if you will, post-traumatic stress disorder—and these are the symptoms of that syndrome. But the reality is that these are also the symptoms of a political crime. People's physical suffering is a consequence of a political crime, and the resolution to that is not always lorazepam. The resolution to that is justice. People need to know that their problems are being dealt with on more than just a technical level. From a medical human perspective, MSF's role is to focus on the human issues and stick to the truth.

MS: And from your personal perspective?
JO: MSF has been a vehicle for my ideals, and it's the right place for me right now.

On the net: student's science exam answers

George Dunea, Cook County Hospital, Chicago, IL

This information came over the Internet some years ago. It purports to be the answers given by students in science exams around the world. It came with the comment that "it is truly astonishing what weird science our young scholars can create under the pressure of time and grades." I was unable to trace the author, but as the work deserves wider dissemination, I present here the answers of most interest to a medical audience.

General

"The body consists of three parts—the brainium, the borax, and the abominable cavity. The brainium contains the brain; the borax, the heart and lungs, and the abominable cavity the bowls, of which there are five—a, e, I, o, and u."

Chemistry

A supersaturated solution is one that holds more than it can hold."

"To collect fumes of sulphur, hold a deacon over a flame in a test tube."

Eyes and nose

"To remove dust from the eye: pull the eye down over the nose."

"For nosebleeds, put the nose lower than the body until the heart stops."

"For a cold: use an agonizer to spray the nose until it drops in your throat."

First aid

"For fainting: rub the person's chest or, if a lady, rub her arm above the head instead. Or put the head between the knees of the nearest doctor."

"For asphyxiation: apply artificial respiration until the patient is dead."

"For drowning: climb on top of the person and move up and down to make artificial perspiration."

"For dog bite: put the dog away for several days. If he has not recovered, then kill it."

Cardiovascular

"The three kinds of blood vessels are arteries, veins, and caterpillars."

"Blood flows down one leg and up another."

Gastrointestinal

"The alimentary canal is located in the northern part of Alabama."

Orthopedics

"The skeleton is what is left after the insides have been taken out and the outsides have been taken off. The purpose of the skeleton is something to hitch meat on."

Reproductive medicine

"Artificial insemination is when the farmer does it to the cow instead of the bull."

"To prevent contraception, wear a condominium."

"Many women believe that an alcoholic binge will have no effects on the unborn fetus, but that is a large misconception."

Hematology

"Before giving a blood transfusion, find out if the blood is affirmative or negative."

Respiration

"When you breathe, you inspire. When you do not breathe, you expire."

"Respiration consists of two acts, first inspiration, then expectoration."

In the Public Eye

Media Watch

The kidney dilemma

Deborah Josefson, *physician and journalist,* San Francisco, CA.
Debdoc.@aol.com

Should a father be allowed to donate his remaining kidney to his ailing child? If the father were a prisoner, would that make a difference? These questions were recently faced by surgeons and medical ethicists at the University of California–San Francisco (UCSF) and Stanford Medical Center in California, sparking a national media debate. A graduate course in law and philosophy at the University of Michigan even asked the question as a final paper project.

The dilemma began in 1996 when David Patterson, serving a 13-year sentence for burglary and heroin possession, donated a kidney to Renada Daniel, the 13-year-old daughter he had abandoned as an infant. Renada was born with congenital renal anomalies and underwent cadaveric renal transplant at age 5. When that transplant failed, she had dialysis for 7 years. In 1996 her father underwent compatibility testing and was found to be the best transplant match. He donated his kidney and thereby renewed his relationship with his daughter. This altruistic donation received national media attention because it required the permission and financial support of prison authorities.

Fast forward to December 1998. Sixteen-year-old Renada was hospitalized at UCSF with an acute rejection episode. During this hospitalization, her father made the unprecedented offer to replace her failing kidney with his remaining one. Transplant surgeons at UCSF refused to consider the offer, but the family insisted. The matter was referred to the hospital's ethics committee.

Medically, the case seemed clear-cut. The removal of Patterson's only kidney would make him dialysis-dependent and shorten his life by about 20 years. Intentionally making someone anephric violates the Hippocratic oath of "first do no harm." So why was the case even considered, and why did it get so much media attention?

Although biomedically the decision appeared obvious, several important ethical considerations were raised. Among them was whether a parent has the right to sacrifice his life for his child. Other wrinkles highlighted by the media included the status of the father as a prisoner, and who would ultimately shoulder the medical costs (dialysis costs at least $40,000 a year). Although her nephrologist, Dr. Donald Potter, denied it, some papers reported that Renada had secretly stopped taking her anti-rejection medications.

Furthermore, because there is a relative shortage of minorities on transplant donor lists, the specter of racial discrimination was raised by the family. Both Renada and her father are African-American. At a press conference in January 1999, a spokesman for the family, the Rev. Lorenzo Carlisle, charged that the ethics committee didn't approve the transplant because Renada and her father are Black, "The child feels that the hospital did not value her black life. If she were Caucasian, they would have approved this," he said (*San Francisco Examiner*, January 21, 1999).

AP Photo/SF Chronicle/Chris Stewart

Renada Daniel-Patterson talks with her father, David Patterson

Vickie Daniel, Renada's mother, contended that the decision was purely a family and spiritual matter in which hospital officials had no right to interfere. In an interview with the *San Francisco Chronicle* (December 5, 1998, p. A17), she said, "I don't know what they are taking so long to think about; they shouldn't have any say-so in this. This man is offering to save his daughter, not their daughter. So, why should this even be a question?" Her viewpoint got some support in biomedical ethical circles.

Hank Greely, chairman for the steering committee of Stanford University's Center for Biomedical Ethics, told the *San Francisco Examiner* (December 11, 1998, p. A2) that parents often make life-threatening sacrifices for their children, and that usually such acts are considered laudable. Moreover, he pointed out that physicians routinely put terminally ill patients through risky and painful treatments that have only a slight chance of increasing the quality and quantity of their lives.

Commenting on the matter, Dr. Wade Smith, a neurologist, and chairman of the UCSF Ethics Committee that deliberated the case, said that from a physician's standpoint, intentionally making someone anephric is "far and beyond anything that the transplant community would accept. The reason it reached the ethics committee is because the transplant surgeon was approached by the family with this request and the surgeon felt very uncomfortable with it. An ethics committee is obliged to answer the questions that are put to it."

"A parent may have the right to run into a burning building, but he has no right to take me with him."

Dr. Smith added that though ethics committee deliberations are usually confidential, much of the debate was in the press because Renada's mother held press conferences on her daughter's condition and the status of the ethics committee deliberations. Although committee deliberations are usually closed even to family members, Renada and her mother were allowed to attend some of them. Dr. Smith found this frustrating. For instance, the committee wanted to make a decision based on the particulars of the case, but the family prevented this. They did not even allow David Patterson to undergo compatibility testing this time around. Since Renada was already rejecting his initial kidney, she might have antibodies against her father's tissue type, which would render him incompatible as a second-time donor.

Moreover, though it's unknown if David Patterson was an IV drug user, he was convicted for heroin possession, and drug users have an increased incidence of renal failure from focal segmental glomerular sclerosis themselves—so the kidney may not have been ideal. However, the family wanted the rule to be a general one, and not merely apply to Renada's case. In reaching its decision, the ethics committee consulted with Mark Fox, an ethicist at the United Network for Organ Sharing, the national organization responsible for maintaining transplant lists, and with Arthur Caplan, a medical ethicist at the University of Pennsylvania. Neither had ever considered such a case before. The committee ultimately ruled that to remove someone's only kidney would be unethical, as it would do unacceptable harm to the donor and would violate the surgeon's own ethics. Dr. Smith said that analogies to a parent running into a burning building to save their offspring were not valid. "A parent may have the right to run into a burning building, but he has no right to take me with him," he said.

The case was not just about a parent's right to save his offspring because it also involved physicians. Because the ruling was a general one, the racial and prisoner status of the donor were not specifically considered. A positive offshoot of the media coverage was that it resulted in more organ donor candidates. In Northern California alone, 3,100 people await renal transplants with an average wait of 3.5 years. For minorities, such as African-Americans, the wait can be even longer because fewer African-Americans volunteer to be donors and also because they have higher rates of diabetes and hypertension, which make them unsuitable donors. The spate of media coverage resulted in over 70 calls from possible candidates and publicized the plight of organ shortages, particularly for minorities.

News and Features

Scientists develop vaccine strategy for peanut allergy

Scott Gottlieb, *New York*

Researchers believe that they may be close to developing a new strategy to combat anaphylactic allergies—such as the increasingly common allergy to peanuts—by inducing tolerance using an oral formulation containing a gene from the offending allergen.

Many established allergies have been traditionally treated by immunotherapy, in which subcutaneous injections of progressively increasing doses of purified allergen are given—a strategy effective in only some circumstances. Dr. Kam Leong, professor of biomedical engineering at the Johns Hopkins School of Medicine in Baltimore, and his colleagues are developing a new strategy to induce allergen tolerance. A gene from the main allergen, in this case peanuts, is cloned into a synthetic vector and administered orally (*Nature Medicine* 1999; 5:380, 387-91).

AP photo/Kathy Willens

Peanut butter sandwiches can kill

The new strategy is based on protecting the allergen's DNA from digestion by forming a complex with particles of chitosan, a naturally occurring polysaccharide that is an effective vector for the controlled intestinal delivery of many pharmaceutical agents. After ingestion, the polysaccharide adheres to the intestinal walls and can be taken in by cells of the gastrointestinal tract. In the latest study, DNA from peanut allergens was administered orally to mice. The severity of anaphylaxis was blunted considerably when the mice subsequently underwent a protocol for sensitization and induction of anaphylaxis using the peanut allergen.

The findings are still a long way from being used in clinical applications. For example, the authors have not yet studied the efficacy of gene administration in mice that are not already sensitized to a particular allergen, which is likely to be the case in humans who would require treatment. "The immune system of mice is also quite different from that of man," said Dr. Leong.

Endostatin may reduce atherosclerosis

Scott Gottlieb, *New York*

An experimental drug known as endostatin, being developed for its ability to shrink cancerous tumors by inhibiting the growth of new blood vessels, is also showing promise in treating atherosclerosis. New research raises the possibility that a new category of drugs—called "angiogenesis inhibitors"—may be useful weapons against heart disease (*Circulation* 1999; 99:1726-32). The researchers found that endostatin significantly reduced atherosclerosis in genetically susceptible mice. In a 16-week experiment on 73 mice, the researchers tested endostatin as well as TNP-470, another substance known to inhibit the growth of capillaries in animals fed a high-cholesterol diet. The mice all had a genetic mutation that made them prone to atherosclerosis. Animals who had been treated with one of the two drugs had 70% to 85% less plaque deposition in their aortas than those untreated. The inhibitors had much less effect if given too early (before the plaques reached substantial size and needed new blood vessels to grow further) or too late (after the plaques were mature).

Endostatin, developed at Harvard University, has been shown to be effective against cancer in animals but has not yet been tested in people. The latest research project was led by Dr. Karen Moulton, a cardiologist, and conducted in the laboratory of Dr. Judah Folkman at Harvard Medical School and at Children's Hospital in Boston. Dr. Folkman pioneered the concept of angiogenesis—the growth of new blood vessels—as a potential target for cancer treatments.

Endostatin is a naturally occurring protein that blocks the formation of blood vessels. Without a blood supply, tumors in animals stop growing and sometimes regress completely. Atherosclerotic heart disease also involves unwanted tissue growth. "By blocking this, perhaps we can alter the progression of the disease," said Dr. Moulton. In addition, cutting off the blood supply to a plaque may reduce the likelihood that the plaque will eventually rupture. Dr. Moulton pointed out, however, that further research is needed to determine whether treatment with angiogenesis inhibitors in people at high risk of heart disease can affect the development of large atherosclerotic deposits.

Ethnic Albanian doctor abducted from her home in Kosovo

see also p.370

Benjamin Hope, *London*

A prominent pediatrician of ethnic Albanian origin was abducted from her apartment in Pristina, Kosovo, according to Amnesty International. Dr. Flora Brovina, one of the few high-profile ethnic Albanians to remain in Pristina, was forced into a car by a group of men, some of them reportedly wearing masks, on April 22. Her brother-in-law, in contact with Amnesty International, had heard no news of her at the time of going to press. Dr. Brovina, 48, was president of the Albanian Women's League, a non-party political organization, and had been involved with local human rights groups and humanitarian work. Last year she had also been active in organizing demonstrations by women to protest against the activities of the Serbian security forces in Drenica. "There are fears that Dr. Brovina may have been targeted because of her activities, which included setting up a rehabilitation center for displaced women and children," said a spokesperson for Amnesty International.

Bone marrow transplants do not help in breast cancer

Scott Gottlieb, *New York*

Preliminary results released early from 4 ongoing clinical studies of breast cancer treatments indicate that high-dose chemotherapy followed by bone marrow transplantation may not significantly improve survival, although positive results from a fifth trial, also released early, seem to suggest otherwise. For almost a decade, ultra-high doses of chemotherapy followed by a bone marrow transplant, to rescue the destruction of the immune system caused by such regimens, has become a preferred treatment in the United States for women with recurrent or advanced breast cancer.

Thousands of women have demanded the procedure. Insurance companies routinely pay for it, even though there is no proof of its effectiveness. Preliminary research released by the National Cancer Institute reflecting 4 of the 5 long-awaited studies of 2,100 women in the US, Scandinavia, and France, found no difference in survival between patients who had high-dose chemotherapy with transplants, and those who had lower doses of chemotherapy.

The fifth study, from South Africa, did find a benefit in patients with positive lymph nodes, suggesting that the treatment might help some women. In this study, 154 women who received the high-dose chemotherapy plus a transplant suffered fewer cancer relapses in the 5-year period following the procedure. After more than 5 years of follow-up, 17% who received transplants had died, as compared with 35% in the other group.

Taken together, the 5 studies are not scheduled to conclude for another 3 to 5 years. Dr Alan Lichter, president of the American Society of Clinical Oncology, said in a conference call with reporters that the lack of conclusive findings thus far in the follow-up suggests that if the procedure does eventually turn out to have a benefit, it will be small. Dr Lichter said, however, these findings might enable better clinical studies, since the early results might "dispel the concern that if you're in a trial and are not on the high-dose arm, you're really missing the boat."

Summaries of the 5 studies are available on the Internet at www.asco.org.

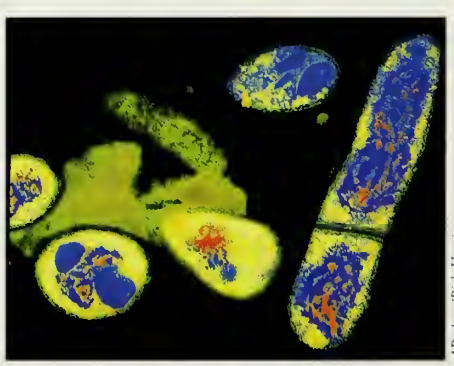
Researchers find genetic basis for susceptibility to mycobacteria

Deborah Josefson, *San Francisco*

Genetics may explain why some people are more susceptible to non-tuberculous mycobacteria infections than others. Researchers at INSERM (National Institute for Medical Research), in Paris, France, investigated the clinical syndrome of disseminated non-tuberculous mycobacterial infection, in which otherwise healthy individuals without detectable immunodeficiency develop overwhelming infections with mycobacteria that are normally not virulent (*Nature Genetics* 1999; 21: 370-8). They uncovered a genetic basis to an underlying susceptibility to infection—one of the few times that discrete, heritable, and spontaneous mutations have been found responsible for making someone vulnerable to a specific microorganism.

Mycobacteria tuberculosis and *M. leprae*—the organisms that cause tuberculosis and leprosy—are the most pathogenic mycobacteria, although most bacteria in their class are relatively harmless. Rare individuals, however, develop disseminated infections with normally non-virulent non-tuberculous mycobacteria. People with the genetic defect can also develop fatal infections after vaccination with *Bacille Calmette-Guérin* (BCG).

The INSERM researchers studied several families with idiopathic reactions to vaccination with BCG or disseminated non-tuberculous mycobacterial infection, including 18 people from 12 unrelated families. From previous investigations, it was known that the receptor for interferon gamma—a cytokine with a central role in combating bacterial, viral, and parasitic infections—was implicated.



AP photo/Rich Harrington

A genetic defect underlies susceptibility to mycobacterial infection

When researchers examined the DNA region encoding the interferon receptor in affected families, they found homozygous mutations in the region, accounting for an autosomal recessive mode of inheritance in some families.

The importance of interferon in combating non-tuberculous mycobacterial infections was underscored by the finding that mutations in genes encoding interleukin 12 (a cytokine that stimulates various cells to secrete interferon) also increased susceptibility. The researchers also found heterozygous mutations in the receptor gene that were inherited in an autosomal dominant manner. This is the first time that autosomal dominant inheritance to a particular pathogen has been found.

Further analysis of these receptor gene mutations showed that they produced a functionally deficient receptor that migrated to the cell surface normally but was unable to respond to interferon. The mutated receptor clogs the cell surface and competes with the normal receptor for interferon binding, further crippling the response to interferon.

US cancer rate declines

Debbie Josefson, *San Francisco*

The overall incidence of new cancers and cancer deaths in the United States fell between 1990 and 1996, but increases in adolescent smoking could reverse this trend, says a new report (*Journal of the National Cancer Institute* 1999; 91:660-1, 675-90). The *Annual Report to the Nation on the Status of Cancer, 1973-1996* confirmed the decline in cancer incidence and mortality first noted last year. Overall cancer incidence dropped by an average of 0.9% per year between 1990 and 1996, and cancer mortality decreased by 0.6% per year.

Incidence data used in the study were culled from 11 population-based cancer registries. They showed that men between the ages of 25 and 44 and over 75 years old had the greatest decrease in the number of new cancers diagnosed, with statistically significant declines in leukemias and cancers of the lung, colon and rectum, urinary bladder, oral cavity, and pharynx. Rates of prostate cancer also declined. Women had statistically significant decreases in new cases of colorectal cancers; rates of leukemias, and oral cavity and pharyngeal cancers also declined. The incidence of breast and uterine cancers remained stable from 1990 to 1996. Deaths from breast cancers declined, however, by an average of 1.7% a year from 1989 to 1996. The only cancers whose incidence increased between 1990 and 1996 were melanomas, up 2.7% per year, and non-Hodgkin's lymphomas, up 0.6% per year.

But the upward trend in teenage smoking threatens to reverse gains made in cancer prevention. Data from the National Youth Risk Behavior Surveillance System showed that smoking increased significantly among high school students, from 27.5% in 1991 to 36.5% in 1997. "Unless we invest now in antitobacco efforts aimed at our youngest citizens," said Donna Shalala, secretary of health and human services, "We will waste the progress achieved so far."

Falsifying data is main problem in US research fraud review

Mark Pownall, *London*

Half of the biomedical researchers accused of scientific fraud in the United States and subjected to formal investigations in recent years are guilty of misconduct, a new review has found. In the biggest review of scientific fraud ever published, the US Office of Research Integrity, has released data on nearly 1,000 allegations investigated from 1993 to 1997. The review covered inquiries into allegations of misconduct in research funded by the US Public Health Service, which has a budget of $15 billion. Altogether, 150 cases were formally investigated after a preliminary assessment of their plausibility. Of these investigations, 76 resulted in findings of scientific misconduct, mostly falsification and fabrication but also plagiarism. Accusations of research fraud most often led to a ruling of misconduct for the least experienced medical researchers, while allegations against full professors and assistant professors less often resulted in guilty verdicts.

Larry Rhoades, director of the division of policy and education in the Office of Research Integrity, said that the figures suggested that "the system is more protective of senior than junior researchers." Senior academics, he said, were more able to defend themselves against accusations. "But we do not know why there are these patterns. We hope researchers might find it interesting to look at these questions." Dr. Rhoades pointed out that those at the academic rank of associate professor, one step below full professor, seemed to attract the most allegations of misconduct. Nearly a third (31%) of the allegations were aimed at this grade, and 17 out of 45 allegations (38%) resulted in findings of misconduct.

Most whistleblowers were senior academics, chiefly professors and associate professors, responsible for about half the allegations. Dr. Rhoades called for international efforts to collect data on scientific fraud, to enable those policing medical researchers to make valid international comparisons.

Scientific Misconduct Investigations 1993-1997 is available from the Office of Public Health and Science, Office of Research Integrity, Suite 700, 5515 Security Lane, Rockville, MD 20852; tel 301-445-5300.

News in brief

Peyote supply shrinks as ranchers withdraw leases *see also p.328*

The supply of Peyote, a mind altering cactus used to promote inward reflection by members of the Native American church, is under threat from ranchers who want to lease their lands for more lucrative business. Peyote is legal for church members, since Congress, backed by the Drug Enforcement Agency, gave people the right to use the drug for religious purposes in 1994. Peyote is claimed to reduce alcoholism rates among Indians—a major health threat in most tribes.

Sex can ward off colds

Levels of IgA, found in saliva and mucosal lining, are raised, albeit slightly, in people who have regular sex, compared with abstainers. In a study from Wilkes University in Wilkes-Barre, presented at the Eastern Psychological Association in Providence, researchers asked 111 undergraduates how frequently they had had sex the previous month and measured levels of IgA in their saliva. The researchers that sexually active people may be exposed to more infectious agents and hence produce more IgA than non-active people.

Oregon judge bans HIV-positive woman from breast feeding

The state of Oregon has ordered an HIV-positive mother not to breastfeed her infant. The mother, Kathleen Tyson, who tested positive six months into her pregnancy, disputes that HIV causes AIDS. Three weeks before giving birth she discontinued her antiretroviral medications and refused AZT during delivery. A temporary court order given previously ordered the Tysons to give their infant AZT for six weeks. The family will be visited to make sure they comply.

Homicide main cause of death for children under one

Homicide, accidental suffocation, motor vehicle accidents, fire, drowning and choking are the main causes of injury related death for children under one, according to a study from the National Institute of Child Health and Human Development. The data were analyzed from linked infant birth and death certificates. Infants were more likely to die from injuries if their mothers were young, unmarried, had lower levels of education, had older children and were Native American or African American. Native American infants were at greatest risk of motor vehicle accidents and drowning.

Medicine and Money

Why HMOs are dumping their Medicaid patients

Scott Gottlieb, New York, NY; sg2@doc.mssm.edu.

The nation's largest health maintenance organizations (HMOs) are quitting managed care programs for the poor and elderly, citing financial losses and continued cuts in government funding. The moves are prompting some patient advocates to fear a return to crowded Medicaid mills, small clinics that generate revenue from high patient volume and low-budget care.

So far, none of California's commercial plans have pulled out of the state's Medicaid program. But Tangerine Brigham, director of policy and planning for the San Francisco Department of Public Health, warned that "state leaders are concerned that in some places reimbursements are so low to providers and health centers that it may be inadequate and force some people to pull out or close their practices and reduce access."

AP Photo/Joel Resnick

ADAPT, a national disability group, demonstrates against Medicaid cuts in Washington DC

"We have to be careful that we don't create a two-tier system where if you are rich you get one kind of treatment and if you are poor you get another kind."

The changes particularly threaten the Medicaid program, where years of declining costs and increasing access to health care for some of the country's poorest patients are in jeopardy of being reversed. HMOs that have already backed away from their commitment to provide health care coverage to recipients of Medicaid include Aetna US Healthcare, Pacificare, Oxford Health Plans, Kaiser Permanente, and Blue Cross/Blue Shield.

One reason cited by the health care plans for the pullouts is recent cuts in state funding for Medicaid managed-care programs. Nationally, state legislators have reduced the per-member monthly rates they pay HMOs by 10% to 20% on average. State Medicaid directors counter that the for-profit HMOs are to blame for abandoning a business they haven't run well. In Portland, Oregon, state officials began requiring Medicaid patients to join HMOs nearly 5 years ago and to submit to rules rationing their health care. But the HMOs couldn't hold down costs, and spending for the plan climbed to $2.1 billion in the 1997-1999 state budget period from $1.7 billion in 1995-1997. Higher cigarette taxes have not offset the increase and the state is now paying more money from its general fund than it did before the program started.

In contrast, problems in Michigan arose after legislators cut the amount of money the state paid to local HMOs. Recently, leaders of Detroit's two largest HMOs warned that sharp cuts in their state's reimbursement rates for Medicaid patients threaten their ability to assure adequate medical care for poor people.

"We have to be careful that we don't create a two-tier system where if you are rich you get one kind of treatment and if you are poor you get another kind," said Gregory Moses, president and chief executive of United American Healthcare Corp., which runs the OmniCare health plan in Michigan. Hundreds of HMOs continue to operate Medicaid programs, and some of the nation's largest HMOs, such as Kaiser and United Healthcare, which have ended programs in some states, have said that they remain com-

mitted to their managed-care programs in other states.

In other cases, managed care plans have continued to cover Medicaid and Medicare recipients but have dropped benefits that they once used to lure clients. In January, none of Maryland's nine HMOs in the HealthChoice program, a state-operated health care program that channels Medicaid recipients into HMOs, passed the state's test for "adequacy of care" for diabetics and new enrollees, who were supposed to be examined within 90 days of signing up. Screening for substance misuse was virtually nonexistent, and it was difficult to tell from records whether patients even had primary care doctors assigned to them.

So far, in California, the commercial HMOs have not defected from the state's Medicaid managed care programs, according to Jamie Tyre, director of business development and marketing at the San Francisco Health Plan. Some plans have recently begun grumbling that they may soon leave, however, according to Jim Lott, executive vice president of the Healthcare Association of Southern California.

Managed care plans are disappointed that they can no longer expect windfalls from insuring Medicaid beneficiaries, and state governments are disappointed that HMOs may not be able to help curtail the rising cost of insuring Medicare and Medicaid recipients.

"Right now, California still is a market with an abundance of providers," Lott said. "So even though capitated payments are 30% less than what they should be, health plans are still able to exact large discounts from hospitals. If that changes, the plans could face more pressure."

Heralding a change in the California market, the state has recently mandated that increases in capitation rates be passed on directly to providers. "Before this decision, that extra money would usually evaporate somewhere at the health plan level," Lott said. Managed care plans are disappointed that they can no longer expect windfalls from insuring Medicaid beneficiaries, and state governments are disappointed that HMOs may not be able to help curtail the rising cost of insuring Medicare and Medicaid recipients. It seems unlikely that the trend to pull out will be reversed.

Blue Cross/Blue Shield of Texas said last month that it will not join the state's Medicaid managed-care program in the busy Dallas area because of what the insurer calls unreasonably low reimbursement rates. "All we were asking for was a break-even on this business, and we were projecting anywhere from a half-million to a $2 million loss," said David Bick, Blue Cross' vice president of government programs.

COMMENTARY

Cost controls must not damage quality

Elaine Batchlor, Vice President, California HealthCare Foundation; ebatchlor@chcf.org
Crystal Hayling, Director, Medi-Cal Policy Institute

The recent exit of managed care health plans from Medicare and Medicaid markets around the country has stimulated heated discussions about the commitment and viability of commercial plan participation in these two government programs. Critics claim that the money-hungry plans have taken their profits and are now abandoning seniors and poor people. Federal and state officials deny that the exits portend challenges or trouble within the programs, citing them as minor setbacks. We will argue that the truth lies somewhere in the middle and aim to point out key concerns and areas where further research is needed.

First, let us begin with the original objective that publicly funded health programs hoped to achieve through the introduction of managed care. Governments implemented managed care in Medicare and Medicaid to provide beneficiaries with increased options for access to quality health care at more affordable prices than in the traditional fee-for-service programs.

There are a number of elements essential to attaining this goal: (1) health plans must continually realize a compelling business case for participation in the programs, (2) beneficiaries must find a compelling reason to enroll in managed care plans or to select one plan over another, and (3) costs must be controlled. It was hoped that managed care plans could do in the public sector what they had shown possible in the private sector: control costs while (arguably to some) maintaining quality.

Use of market mechanisms to improve access and control costs requires acknowledging some of the realities of how markets function. Entry and exit is a natural part of properly functioning markets. The question should not be whether exits will occur, but why plans are leaving and the extent to which beneficiaries are affected.

Although some plans say they are exiting markets because of inadequate rates and burdensome regulations, there may be additional reasons. Some plans entered markets late and found they couldn't build enough market share to make the business viable. Other plans may have failed to develop the expertise

needed to make the programs work. The important questions are whether a sufficient number of high-quality plans remain in the market to achieve the goals of the programs and whether the level of instability presents an unacceptable level of disruption in patients' care.

In order for the managed care marketplace to work, it must also be financially viable for physicians. If premiums are too low, physicians will be unable or unwilling to participate in the program. There are signs that payments to physicians may be too low in some places.

Some physicians, particularly in California, where physician payments are relatively low, say they are teetering on the edge of financial inviability. As one factor influencing plans' decisions to leave markets, plans cite resistance from physicians who are holding the line against rates they say are too low to deliver quality care. Other plans are reconfiguring their networks to exclude, where possible, physicians who demand higher payments. Instability among physicians participating in the programs may cause greater disruption of patient care than the exit of health plans.

Finally, there are powerful forces causing medical costs to increase every year. The major drivers toward cost increases are the development of expensive new technology, pharmaceuticals, and the aging population. Payments to plans and physicians need to keep pace with some of these dramatic increases in medical costs. Yet federal and state budget decisions frequently have more impact on rates than do business decisions based on program costs.

For the Medicare program, the Balanced Budget Act of 1997 established a 2% cap on health plan payment increases at a time when medical costs were projected to rise 6% a year. Risk adjustment, scheduled to start in the year 2000, has added uncertainty to the question of future rates. This raises the question of whether rates will be adequate to support the business case for plans to participate in the program and what changes plans may make in order to stay in the program.

In the Medicaid program, federal guidelines impose an 'upper payment limit' that prevents states from paying more for managed health care than they would have paid under fee-for-service. In California, where fee-for-service rates were low prior to the implementation of managed care, health plan capitation rates are currently the lowest in the nation. Physicians and plans complain about these low rates which, prior to 1998, had not been increased significantly in more than a decade. Admittedly, states must be frugal purchasers. But if low rates cause a constant seepage of physicians and plans from the system, state leaders may find that they have undermined the very system they created.

The forces driving increased medical costs make it imperative for governments to have a mechanism for controlling costs without jeopardizing access to quality care.

And what about the beneficiaries? How much have recent plan pullouts affected their care and what can they expect in the future? In the Medicare program, the number of beneficiaries that have been affected has been a relatively small percentage of the total. Many of the plan terminations were in rural areas where managed care enrollment and rates have been low. Most beneficiaries enrolled in plans that terminated had the option of joining another managed care plan, although that may have meant changing doctors. In California, for example, only 0.5% of beneficiaries, or about 6,600 people, were left without the option of joining a managed care plan.

Managed care plans originally used generous government premiums to add benefits such as prescription drug coverage and low out-of-pocket costs to attract beneficiaries. This resulted in rapid growth in enrollment. Plans' response to less generous premiums may be to decrease drug benefits and increase enrollee cost-sharing. Plans will attempt to do this while continuing to differentiate managed care from traditional Medicare and supplemental plans enough to appeal to beneficiaries. The outcome for enrollees in Medicare managed care is likely to increase out-of-pocket costs.

More information is needed to understand exactly what health plan exits from Medicare and Medicaid signal for future health plan decision-making, physician participation, and beneficiary care. The Medi-Cal Policy Institute, a project of the Foundation, has embarked on a study to examine the financial viability of health plans involved in the Medi-Cal program in order to understand how past performance may impact future behavior.

The forces driving increased medical costs make it imperative for governments to have a mechanism for controlling costs without jeopardizing access to quality care.

Managed care is the primary approach currently on the horizon that offers the possibility of achieving this goal. This creates a strong case for figuring out how to make it work for plans, physicians, the government and, most importantly, beneficiaries.

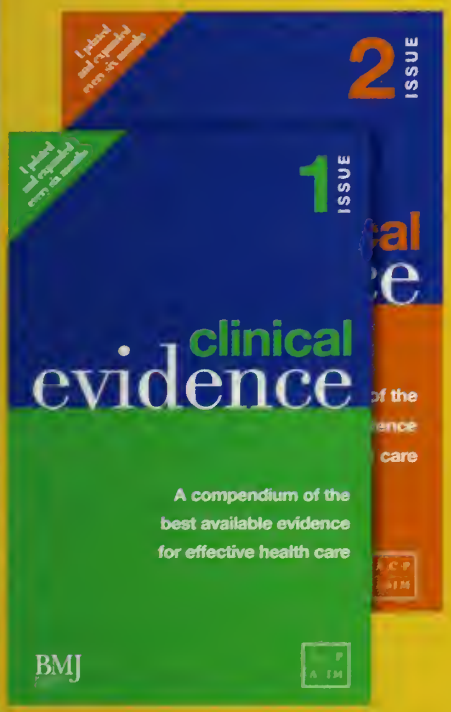
capsule

Affluence doesn't always improve survival. Adults with cancer do better if they are affluent, and there is some evidence that the same is true for children. An international team of researchers reports, however, that there is no socioeconomic gradient in children's survival from acute lymphocytic leukemia (*Archives of Disease in Childhood 1999;* 80:311-7). The researchers linked cancer registry data from England and Wales with measures of deprivation and found only a 3-6% difference in survival between socioeconomic groups—no more than would be expected by chance.

NEW IN 1999

Clinical Evidence

from ACP-ASIM and BMJ Publishing Group



Published in convenient reference format for ease of use, Clinical Evidence is available by subscription in US and UK editions.
A sample section of Clinical Evidence is available for you to view on the web at: www.evidence.org.
Subscribing couldn't be easier, simply complete the order form below and return with payment to the address provided.

Clinical Evidence **is a compendium of evidence on the benefits and harms of common clinical interventions. Written by practising clinicians using rigorous searching and evaluation methods, it will be issued every six months to bring you the most reliable and up-to-date findings on important questions in clinical practice. *Clinical Evidence* will be published as a convenient reference book in order to make clinical effectiveness accessible and possible for health professionals worldwide.**

Clinical Evidence **will enable clinicians and health care professionals to make informed decisions about:**

- Choosing one treatment or test over another
- Informing patients and their families, and involving them in decision making
- Identifying gaps in the evidence
- Conducting and commissioning research
- Auditing clinical procedures
- Resolving disputes over efficacy of treatment
- Training clinicians, managers and students

The first issue will contain:

- Breast Diseases
- Cardiovascular Diseases
- Child Health
- Diabetes
- Digestive System Diseases
- Diseases of Ear, Nose & Throat
- Eye Diseases
- Gynaecological Disorders
- Infectious Diseases
- Mental Health
- Musculoskeletal Diseases
- Neurological Diseases
- Respiratory Diseases
- Wounds
- Skin Diseases
- Sexual Health
- Urinary Tract Disorders

---

linical Evidence
)99 Subscription rates - Regular rate: US$99
CP-ASIM member rate: $89 Institutional rate: $192
ıstitutional rate applies to any library or organisation buying for the use of ore than one person)
:udent rate: US$53 (Students please provide proof of student status)
ublication: Six monthly

lease tick which edition you would like to receive)
] US edition (first issue available October 1999)
] UK edition (first issue available June 1999)

ease tick:
] I enclose a check for $ .....
(Payable to British Medical Journal. US dollar checks to be drawn on a USA bank account)
] Charge my credit card $ .....
American Express / Visa / MasterCard / Delta
ardholders No
☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐

xpiry Date:.....Signature: .....

Name: .....

Job title: .....

Address: .....

.....

Country: .....Postcode: .....

E-mail Address: .....

☐ Please tick if you do not wish your data to be used for direct marketing purposes

Return to: BMJ Publishing Group, Box 590A, Kennebunkport, ME 04046, USA
Tel: 1-800-2-FON-BMJ Fax: 1-800-2-FAX-BMJ
Email: bjpaige@cybertours.com

N.B. Subscribers in Canada must add 7% GST to the quoted dollar price unless they can provide a registration number

Visit our website at: www.evidence.org

BMJ

ACP ASIM

Speaker's Corner

Unnerving: a patient's view of the debate over prostate cancer

"For in much wisdom is much grief: and he that increaseth knowledge increaseth sorrow."—Ecclesiastes 1:18

I came to that very same conclusion a couple of years ago when I discovered the disagreements among doctors over screening and treatment of prostate cancer.

In retrospect, I'm not sure if I'm better or worse off for having found out that many of the learned heads in the field are having serious disputes. It's unnerving when you stumble across something like that. It's sort of like having the door to the cockpit of your 737 suddenly swing open, and you witness 2 pilots arguing vehemently about the flight plan.

Especially unsettling was the discovery that doctors have big egos and big emotional investments in their own ways of doing things. Sometimes the scientific method winds up in the back seat. This fact was brought home to me when I was evicted from a world-famous university hospital by uniformed security guards because a renowned surgeon took offense during an interview when I questioned whether prostatectomies actually save lives.

Let's start at the beginning. After my 50th birthday I visited my internist for that dreaded "the times they are a-changing" examination. The only discordant note was that the physician detected a little "asymmetry" in my prostate. My prostate wasn't hard. It wasn't swollen. Just a tad lopsided. Before leaving the office, I had in my hand a lab referral slip for a prostate specific antigen (PSA) test. Until that time, I had only associated the acronym "PSA" with the now-defunct airline that once flew cheap, reliable passenger service up and down the West Coast from its home base in San Diego.

Even though my test results came back normal, indicating no sign of cancer, my internist referred me to a specialist, just to be on the safe side.

A week or so later I visited a urological practice on Telegraph Avenue in North Oakland. Another digital rectal examination confirmed the asymmetry. As for the PSA result, the urologist dismissed it. "You can have a normal PSA and still have cancer." That was the first shock.

He recommended another round of tests. First, a sonogram, to take a Polaroid picture of the prostate for closer examination. And if that were to prove inconclusive, the next test would be a biopsy. The word "biopsy" has a way of focusing the mind. At this point, I could have said no. The thought just never occurred to me. The next thing I knew, I was standing at the counter in a pharmacy, purchasing a brace of Fleeta enemas to prepare me for the next plateau. The testing procedures were, as physicians say with considerable understatement, invasive. The sonogram was inconclusive, and so the urologist performed the biopsy.

It involves insertion of a wire-like cable up the rectum. At the end of the cable is a razor-sharp set of jaws that are cocked open. After the physician guides it into place against the prostate, he trips the release. Bingo! The minutes awaiting the six clicks of the cable release collecting the specimens of my prostate were among the longest I've spent on this earth. No anesthesia was involved. After it was over, the nurse showed me a beaker full of fluid in which 6 raw bits of my tissue floated lazily to the bottom.

When I returned to the urologist's office for the results of the biopsy, I was apprehensive. A fog lifted when he told me the biopsy was negative. As a precaution, however, he urged me to continue with PSA testing every year.

When I walked out of the office, I first felt liberated, but also profoundly confused. My welcome to the promised land of "early screening" had been anything but reassuring.

Shortly afterward, I shared my experiences with the producers of Soundprint, a public radio program with an emphasis on science. I proposed doing a half-hour radio documentary on prostate cancer, based somewhat on my own experience, as an alert to men my age.

When my proposal was accepted, the door opened to several months of intensive research.

In interviewing many of the leading figures in the field and reading up on the literature, I caught a glimpse of the medical world that patients seldom see. It's not the brave face of conviction and confidence that one usually sees in the clinician. Instead, it's a world fraught with controversy, disputes over research results, and questions that won't go away: What about the efficacy of the PSA test? What about the advisability of the increasingly popular radical prostatectomy? What about the studies from Scandinavia apparently showing that surgery was no more effective in saving lives than watchful waiting?

When I raised these questions with a world-renowned specialist in the field, the interview ended after 20 minutes. The surgeon picked up his telephone and called security to have me removed from the building. For a fleeting moment, I felt like the character Harrison Ford plays in the movie *The Fugitive* as I crept around the frozen streets, attempting to sneak back into the hospital to finish my interviews.

When I completed the documentary, I had a small sense of satisfaction that I was able to send up a warning to listeners to be wary of the sweeping claims made about prostate cancer treatment. I became keenly aware of any and all media reports on the topic. The ones that gave me the most concern were those that uncritically endorsed PSA testing and prostatectomy as a remedy for prostate cancer.

Only regular readers of the *Wall Street Journal* would be aware of the very large financial implications of this debate. The PSA test costs around $50. Multiply that by the millions of men over age 50 who might be persuaded that a yearly PSA is a good idea. There is the possibility that the number of prostatectomies could grow to 100,000 per year, without any scientific proof so far that this kind of surgery prolongs life any better than watchful waiting.

I'm just not sure that I'm better off knowing all these things.

William J Drummond
wdrummon@uclink4.berkeley.edu

William J. Drummond is a professor of journalism at the University of California-Berkeley. He reports occasionally for public radio. His public radio documentary, "It's a guy thing: plain talk about prostate cancer," is available through www.soundprint.org/.

Mass immunization: did we do more harm than good?

see also p.392

David Heiden

By 1983 the health care system in Uganda was in shambles. It was the immediate aftermath of Idi Amin, and during his 10-year rule, the childhood immunization program had fallen apart. Measles was the leading reported cause of death in the country, and more hospital beds were occupied by patients with measles than for any other disease.

I was there to help restart primary immunization—measles, polio, DPT, and BCG. We knew we were doing something that was needed because almost every day we saw children with withered limbs from polio. In a month we had trained several teams and immunized about 25,000 children. But thinking back on the experience makes me reflect on the complexity of even something as simple as immunization, and the ever-lurking possibility of good intentions leading to more harm than good.

For example, on our third morning we discovered a problem with the "cold chain." The cold packs had been put in the refrigerator instead of the freezer, and they weren't frozen. Without frozen cold packs we couldn't keep measles vaccine viable in the equatorial African heat. At 9 AM we put the packs in the freezer, but by 2 PM they still weren't frozen. It was 4:30 when I finally arrived at the Busia market, the morning immunization site, to explain that the vaccinations had to be cancelled. The local nurse said that there had been an excellent turnout, about 1,000 children and mothers, plus the village chief, schoolteachers, and clergy, who had been working for weeks to remind and encourage everyone to come. But now, all the people were gone. The crowd had arrived at 8 AM. It had been hot. There was no water and no lunch for the children. The nurse said that the chief had made very nice speeches about immunization all morning, trying to keep the people patient. At noon they sent everyone on foot to the afternoon site 6 miles away. By the time we drove to the afternoon site, everyone was gone except for 6 men sitting in a hut drinking Pombe, the local homemade beer.

Then, in the second week, something worse happened. We drove 2 hours over rutted dirt tracks to reach the appointed village. We unpacked, only to discover that we had left the box of needles behind. The local schoolteachers and village priest who had organized the turnout and had dressed in their best clothes greeted us with nervous eagerness and pride. They had done wonderfully: there were 700 children crowded into the village center. Again, many of the mothers had come 5 or 10 miles on foot.

A teacher administering oral polio vaccine

But we had only two needles. We argued about what to do but finally went ahead, reusing the same 2 disposable needles on 700 children. We didn't know that by 1983 HIV infection had taken hold in Uganda. I can't help wondering if we contributed to the epidemic by our work that day.

—David Heiden, *ophthalmologist, San Francisco*

Letter from the Southwest

A medicine man and a lesson learned

Mark Carroll, Flagstaff, AZ, mcarroll@infomagic.com

Culture in health care creates both obstacles and opportunities. A weekly field clinic in a remote Navajo community helped us understand the obstacles: unpaved roads, unpredictable skies, and unfamiliar "Western" diagnoses and treatments. Rising rates of chronic disease and flagging patient compliance pressed us to identify an opportunity—the medicine man. Anxious to bridge cultural traditions with modern disease management, we designed an integrated clinic that included, instead of competed with, the traditional healer. We set out to select our new colleague.

Picture an open, unspoiled space, accessible only by 40 miles of snaking, cracked pavement and 10 miles of sometimes graded, always washboarded clay. Multicolored mesas stand like sentinels against the southern sky. Grasslands struggle to recover from decades of confined grazing and one devastating year of drought. People live here—*the people*, the Dine. They live in mud and juniper-pole hogans, sun-bleached trailers, unpretentious wood frame buildings. We make the 50-mile trip here every Tuesday, and unlock an earth-toned trailer that, except for the fencing around it, might be someone's home. It is our clinic.

"Do you know a medicine man we might hire?"

We polled some community members, people who work with us in the hospital at Tuba City. Our goal, we explained, was simple: hire a medicine man to see patients with us each Tuesday. Would we build him his own hogan? Sure. How would we refer patients to him? We would tell patients he was there. What would be his role? He would meet with people, pray with them. Perhaps, in the process, patients might feel better motivated to take their diabetes and high blood pressure medications, to be more careful about their diets, or to lose extra pounds that could prevent heart disease or kidney failure.

"Do you think it will work?"

Our coworkers were unsure. We would need to pay the medicine man well. We would also need to be careful who we hired and how. Choosing one medicine man might upset others who were not selected. We decided to consult a medicine man from another community, someone not likely to be biased by the possibility of being hired into our project.

On weekdays, "Martin" works as a counselor; on weeknights and weekends, he is a traditional healer. He is a humble man, tall, lean, and soft-spoken. I dropped by his office, and described the project to him. He asked why I thought a medicine man could help.

Dance of the Deer Foundation, Center for Shamanic Studies, Soquel, CA

Huichol Indian yarn painting, promoting health and healing

"We are trying to integrate approaches. We don't understand—culturally—why and how people decide to take medicines, to keep appointments, to generally take care of themselves. A medicine man might help us reach out. He might help patients trust us."

Martin nodded. He noted the logistical difficulty of combining traditional diagnosis and ceremony into one brief visit to a medicine man. He wondered how the people seeing the medicine man would be able to commit themselves to their healing, and how their families, their clans, would be able to support and share in that commitment. I explained the urgency of the health problems. But healing, Martin shared softly, is more than rushed ritual. It is a process, a journey made by patients with their families, their community. How the journey is made matters. We sat without speaking. I had assumed Martin would embrace the proposed clinic as a productive step toward the inevitable integration of traditional and "Western" medicine. Suddenly, in the silence following our exchange, I understood the arrogance of that assumption.

"Western" medicine's logic—(1) Navajo people believe in medicine men; (2) medicine men are expensive; (3) if we pay for medicine men, more Navajo people may trust us and listen to our advice—is based on manipulative misunderstandings of traditional Indian healing. Such misunderstandings do not promote integration; they undermine it. Yes, Navajo people see the markings of culture—head-banded healers, smoke-filled hogans, corn pollen paintings. Yes, they hear the swirling chant of ancient song, when they sit cross-legged on well-tamped ancestral earth. But they also see the gifts—blankets, baskets, prepared food—donated and blessed by the extended family that made and gave them. In the midst of a healing ceremony, in the center of song and ritual, people feel a circle of support surrounding them, a network of community caring about them, believing in their ability to be healed. Identity and a sense of connectedness is recovered inside these circles. As the heart of healing, it cannot be replaced. As the essence of culture, it should never be purchased.

"Integrating" alternative approaches to health care involves more than juxtaposing one healing tradition alongside another. Belief systems—cultural traditions—are neither remediable mistakes (obstacles) nor manageable resources (opportunities) amenable to well-intentioned molding. They are who people are. They are what make our differences vital.

Classified Advertisements

The rate for each insertion is $1.50 per word, with a minimum of 30 words ($45). A word is defined as one or more letters bounded by spaces. Bold type face is available at no extra charge. Confidential box numbers are available for an extra $10 per insertion. Classified advertisement are payable in advance by check, AMEX, VISA or MasterCard.

To place your ad, contact:
Ruth Staunton,
WJM Western Journal of Medicine,
221 Main Street, PO Box 7690,
San Francisco, CA 94120-7690,
Tel 415-974-1071, Fax 415-882-3379
rstaunton@bmjgroup.com

Classified Display Advertising

The classified display rate is $70 per vertical inch. Maximum sizes: 1 column by 5 inches or 2 columns by 2 inches ($2\frac{1}{8}$ inches per column). Larger classified ad space available on request. Please supply camera-ready artwork if logos or other art are included in the ad. Copy for classified advertisements should be received no later than the first of the month preceding issue. All copy must be typed or printed, we prefer to receive copy electronically as e-mail or on a disk.

MEETINGS/CONFERENCES

The ACC/SCA&I Board Review Program: Interventional Cardiology, October 14-17, 1999, the Westin Peachtree Plaza, Atlanta, Georgia. Sponsored by the American College of Cardiology, and the Society for Cardiac Angiography and Interventions. Program Directors: George W Vetrovec, MD, FACC, FSCAI, and Morton J Kern, MD, FACC, FSCAI; 21 category 1 credit hours. **Information:** 800-253-4636, ext. 695, fax 301-897-9745.

WESTERN STATES OPENINGS

Many multispecialty groups and hospitals have asked us to recruit for over 100 positions of various specialties. Both permanent and locum tenens. Send CV to:

Western States Physician Services
7510 No. Trellis Circle, Fresno, CA 93720
Call 800-873-0786, fax 800-705-7943
e-mail weserve@lightspeed.net

★ ★ ★ ★ ★ ★ ★ ★ ★ ★

ENJOY A SEASIDE VACATION IN SAN DIEGO!

San Diego Academy of Family Physicians' 43rd Annual Postgraduate Symposium
"Family Medicine Update: 1999"
Hotel Del Coronado • Coronado, California
July 9-11, 1999

This SDAFP Symposium features a variety of educational lectures and specialty workshops. This program has been accredited by the AAFP for 19 Category 1 CME credit hours. The SDAFP is an approved provider for this program by the AOA, AAPA, and Boards' of Pharmacy and Registered Nursing.

Many entertaining social activities have been planned for the whole family, so don't miss this opportunity to combine top quality continuing medical education with a fun family vacation.

To receive a detailed brochure, call, fax or write to:

SAN DIEGO ACADEMY OF FAMILY PHYSICIANS
P.O. Box 5996, Chula Vista, California 91912
(619) 422-1186 FAX (619) 476-1536

PHYSICIANS WANTED

Northern California Wine Country: Mendocino Community Health Clinic seeks caring, motivated individual for work in clinic and hospital, including ICU. NO OB. Pure air, gorgeous country, 40 minutes to coast, 2 hours to SF. No managed care. Superb compensation. No J1 positions available. Fax resume to Carole Watkins, Director of Human Resources, 707-468-0174.

Northern California: Opportunity in Small University Community. Prime area to raise family. Great recreation area for all seasons. Family Practice or Internal Medicine Physician needed for Urgent Care Clinic and Family Practice. **Contact:** Fax CV to 530-897-3758.

Busy growing Community Health Center needs a Board Eligible/Certified Family Practitioner. OB is optional. Spanish skills helpful. **Contact:** Peggy Leitner, 303-665-9310 for more information.

Salem/Willamette Valley–Salem Clinic, PC: a 40-physician multi-specialty group located in Salem, Oregon, is currently recruiting a full-time Internal Medicine physician. The position consists of a $4\frac{1}{2}$-day workweek. Salem Clinic offers a comprehensive benefit package and competitive income guarantee with opportunity for rapid incorporation into production formula. 1:7 call, single hospital town. If interested, please forward, fax or e-mail a copy of your CV. **Contact:** Sherry Krog, Salem Clinic, PC, 2020 Capitol St. NE, Salem, OR; 503-399-2470, fax 503-375-7429, e-mail gunderBL@aol.com.

California–Monterey Bay: Full/Part-time positions. 12 clinic urgent care system seeking BC/BE, EM/FP physicians. Work 2-3 days/week with 4-5 days off! Benefits include competitive compensation, malpractice insurance paid, 401k & health insurance. Practice in California's most beautiful coastal recreational area. **Contact:** Donaldo M Hernandez, MD at 831-622-8400; Send CV to Medical Director, Doctors on Duty, 100 Clock Tower Pl., #220, Carmel, CA 93923; fax 831-622-8401, or e-mail mmcmilla@doctorsonduty.com.

IM/FP, BC/BE, Post Falls, ID: Rapidly growing Primary Care practice. Possible part-time. Hospital privileges required. Salary 3-6 mos, then production. Need WA&ID licenses. **Contact:** Michael Carraher MD, 208-773-0721.

Continuing Medical Education

ARIZONA ● CALIFORNIA, HAWAII, NEVADA ● COLORADO ● IDAHO ● NEW MEXICO ● UTAH ● WASHINGTON ● WYOMING

ARIZONA

All courses listed have been certified as meeting the criteria for Category I of the ArMA CME Certificate and the AMA Physicians Recognition Award. To list Category I CME programs, please send information to Arizona Medical Association, 810 West Bethany Home Road, Phoenix, AZ 85013; or phone 602-246-8901.

Brochures and registration forms are available from the contact person or organization sponsoring the program.

OCTOBER 29–31, 1999: Neurology for the Non-Neurologist. The Phoenician, Scottsdale, AZ. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; tel 800-421-3756; fax 303-798-5731.

DECEMBER 10–12, 1999: Managing Respiratory Disease. The Phoenician, Scottsdale, AZ. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; tel 800-421-3756; fax 303-798-5731.

CONTACT INFORMATION

Mayo Clinic-Scottsdale Contact: Postgraduate Courses, Mayo Clinic-Scottsdale. Phone 602-301-7447.

U of A Contact: University of Arizona College of Medicine, Arizona Health Sciences Center, Tucson, AZ 85724. Phone 520-626-7832 or 800-328-5868.

CALIFORNIA, HAWAII, AND NEVADA

All courses and meetings listed are approved for Category I credit toward the CMA Certificate in CME. To list accredited courses here, please send information at least two months in advance to Paulette Richardson, Continuing Medical Education, California Medical Association, PO Box 7690, San Francisco 94120-7690; or phone 415-882-3387. For more information on accreditation or certification, please write to the above address.

ALLERGY/IMMUNIZATION

AUGUST 13–15, 1999: A Midsummer Night's Wheeze. California Society of Allergy, Asthma and Immunology at La Costa Resort and Spa, Carlsbad, CA. 12 hrs. $145-$199. Contact: CSAAI Conference Management; tel 714-828-8022.

ANESTHESIOLOGY

NOVEMBER 5–7, 1999: 11th Annual Anesthesiology Update. Monterey Plaza, Monterey, CA. Contact: tel 916-734-5390.

NOVEMBER 4-6, 1999: UC Otolaryngology Update 1999. UCSF at Ritz-Carlton Hotel, San Francisco, CA. 18.5 Cat I hrs. $425. Contact: tel 415-476-5808.

CARDIOLOGY

JULY 25-29, 1999: Nineteenth Annual Current Concepts in Primary Care Cardiology. UC Davis School of Medicine, Division of Cardiovascular Medicine. Granlibakken Conference Center, Tahoe City, CA. Contact: Kimber Chavez, Program Representative; tel 916-734-1394; kimber.chavez@ucdmc.ucdavis.edu.

OCTOBER 7-9, 1999: 23rd Annual Cardiology Update 1999. American College of Cardiology at Carmel Valley Ranch Resort, Carmel, CA. 12 Cat. I hrs. Contact: Registration Secretary, Extramural Program Dept., American College of Cardiology; tel 800-253-4636, ext. 695; fax 301-897-9745.

OCTOBER 13-17, 1999: Coronary Interventions 1999. Scripps Clinic at Hilton La Jolla Torrey Pines, San Diego. Contact: Jill Hofmans, Conference Services Supervisor, Scripps Clinic. Dept. of Academic Affairs, 403C. 10666 N. Torrey Pines Rd., La Jolla, CA 92037; tel 619-554-8556; fax 619-554-6310.

EMERGENCY MEDICINE

AUGUST 16–19, 1999: National Emergency Medicine Board Review. American College of Emergency Physicians at Harrah's Las Vegas, NV. 40 hrs. $895. Contact: Center for Emergency Medical Education; tel 800-651-CEME (2363).

OCTOBER 3-5, 1999: Northern California Trauma Center Conference. UC Davis at Hyatt Regency, Sacramento. Contact: UC Davis; fax 916-734-4298.

OCTOBER 28-31, 1999: California Board Review. A Comprehensive Review of Emergency Medicine. American College of Emergency Physicians at Paradise Point Resort, San Diego, CA. 50 hrs. $895. Contact: EMEDS; tel 888-616-1711.

ENDOCRINOLOGY

OCTOBER 22–24, 1999: Clinical Endocrinology for Primary Care Physicians. Tropicana, Las Vegas, NV. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; tel 800-421-3756, fax 303-798-5731.

ETHICS

SEPTEMBER 22-25, 1999: Legal Issues in Damaged Brain Injury Cases. UC Davis at Westin St. Francis Hotel, San Francisco, CA. Contact: UCD; tel 916-734-5390.

FAMILY PRACTICE/PRIMARY CARE

JUNE 25-27, 1999: Dermatology for the Non-Dermatologist. Medical Education Resources at the Hyatt Regency Alicante, Anaheim, CA. 11 hrs. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Ct., Ste. 500, Littleton, CO 80120-4569; tel 800-421-3756.

JULY 5–8, 1999: Family Practice Board Review Course. UCSF at Fairmont Hotel, San Francisco, CA. 25 hrs. $525–$575. Contact: Program Coordinator, Dept. Family and Community Medicine, 500 Parnassus Ave, MU-3E, SF, CA 94143-0900; tel 415-476-5250.

JULY 17-18, 1999: 3rd Annual Primary Care Pediatric Orthopedics. Valley Children's Hospital at Doubletree Hotel, Monterey. 8 hours. $150. Contact: William Hennrikus; tel 559-353-5944.

JULY 23-24, 1999: Controversies in Women's Health. UCLA at Disneyland Hotel. 12 hours. $75-125. Contact: Jean Abbott; tel 310-312-0531.

NOTICE

State Associations should send their CME listings for publication to:

Catherine Nancarrow, Editorial Manager,
WJM Western Journal of Medicine,
PO Box 7690, San Francisco, CA 94120-7690;
tel 415-974-5977; fax 415-882-3379;
wjmsf@pacbell.net.

JULY 25–29, 1999: 19th Annual Current Concepts in Primary Care Cardiology. UC Davis at Granlibakken Conference Center, Tahoe City, CA. Contact: UCD; tel 916-734-5390.

JULY 30–AUG 1, 1999: Coronary Heart Disease Update. Medical Education Resources at Tenaya Lodge, Yosemite, CA. 11 hrs. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Ct., Ste. 500, Littleton, CO 80120-4569; tel 800-421-3756.

AUGUST 6-8, 1999: Managing Respiratory Diseases. Medical Education Resources at the Hyatt Regency Monterey, CA. 11 hrs. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Ct., Ste. 500, Littleton, CO 80120-4569; tel 800-421-3756.

AUGUST 20-22, 1999: Primary Care Medicine. Scripps Clinic at Coronaro Island Marriott Resort, San Diego. 16 hours. Contact: Cheryl Trinidad, conference Coordinator, Scripps Clinic, Dept. of Academic Affairs, 403C, 10666 N. Torrey Pines Rd., La Jolla, CA 92037; tel 619-554-8556; fax 619-554-6310.

OCTOBER 2-4, 1999: 7th Annual Western Retreat: Practical Primary Care. Scripps Clinic at Monterey Marriott. 12 hours. Contact: Cheryl Trinidad, conference Coordinator, Scripps Clinic, Dept. of Academic Affairs, 403C, 10666 N. Torrey Pines Rd., La Jolla, CA 92037; tel 619-554-8556; fax 619-554-6310.

OCTOBER 22-24, 1999: Clinical Endocrinology for Primary Care Physicians. Medical Education Resources at the Tropicana Hotel in Las Vegas, NV. 11 hours. Contact: MER Linda Main, Meeting Coordinator, 1500 West Canal Ct., Ste. 500, Littleton, CO 80120-4569; tel 800-421-3756.

OCTOBER 28-31, 1999: 11th Annual CME/Golf Meeting. Nevada Academy of Family Physicians at The Orleans Hotel & Casino, Las Vegas, NV. Contact: Barbara Bolling, NAFP, P.O. Box 27713, Las Vegas, NV 89126-1713; tel 702-228-5852; nafplvbb@aol.com.

INTERNAL MEDICINE

AUGUST 22–27, 1999: New Advances in Internal Medicine. UC Davis at Embassy Suites, Monterey, CA. Contact UCD; tel 916-734-5390.

OB/GYN

SEPTEMBER 25–26, 1999: Ultrasound Update, 1999. Hilton Hotel, Sacramento, CA; 916-734-5390.

DECEMBER 10–12, 1999—Issues in Women's Health. Tropicana, Las Vegas, NV. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; tel 800-421-3756; fax 303-798-5731.

OCCUPATIONAL & ENVIRONMENTAL

AUGUST 5-6, 1999: Occupational & Environmental Toxicology for the Health & Safety Professional. UC Berkeley. Holiday Inn Bay Bridge, Emeryville, CA. Contact: Center for Occupational & Environmental Health, UC Berkeley, Richmond Field Station, 1301 S. 46th St., Bldg. 102, Richmond CA 94804; tel 510-231-5645; http://socrates.berkeley.edu/~cochce/.

SEPTEMBER 23-26, 1999: Western Occupational Health Conference (WOHC). American College of Occupational and Environmental Medicine and the Western Occupational and Environmental Medical Association at Monte Carlo Resort and Casino, Las Vegas, NV. 21 hours. Contact: Justine Abel, WOHC, 74 New Montgomery, Suite 230, San Francisco, CA 94105-3411; tel 415-764-4083; fax 415-764-4915; woema@hp-assoc.com; www.woema.com.

ONCOLOGY

SEPTEMBER 17-18, 1999: 5th Annual Cancer Research Symposium. UC Davis at Cancer Center Auditorium, Sacramento, CA. Contact: Office of CME, UC Davis Medical Center, 2315 Stockton Blvd., Camellia Cottage, Room 1019, Sacramento, CA 95817; tel 916-734-5390; fax 916-734-8966.

OCTOBER 14-16, 1999: 23rd Annual Physicians Cancer Symposium. Scripps Health, Stevens Cancer Center, San Diego, CA at La Jolla Hyatt Regency Hotel. 16.5 CME hours. Contact: Ruthanne Crawford, Stevens Cancer Center, Scripps Memorial Hospital 9888 Genesee Avenue, La Jolla, CA 92037; tel 619-626-6756; fax 619-626-6793; racrawford@ch2.edu.

OCTOBER 14-16, 1999: 19th Annual Nurses Cancer Symposium. Scripps Health, Stevens Cancer Center, San Diego, CA at La Jolla Hyatt Regency Hotel. 18 contact hours. Contact: Ruthanne Crawford, Stevens Cancer Center, Scripps Memorial Hospital 9888 Genesee Avenue, La Jolla, CA 92037; tel 619-626-6756; fax 619-626-6793; racrawford@ch2.edu.

PEDIATRICS

JULY 16–17,1999: Seventh Annual Pediatric Update. Sponsored by Lucile Packard Children's Health Services at Stanford and faculty from UCSF and Stanford Schools of Medicine. Lucile Packard Children's Hospital. Contact: Elinor Meyer, Continuing Medical Education and Physician Relations Department, Lucile Packard Children's Hospital, 725 Welch Road, Palo Alto,CA 94304; tel 650-497-8554.

PRIMARY CARE

JULY 25–29, 1999: 19th Annual Current Concepts in Primary Care Cardiology. Granlibakken Conference Center, Tahoe City, CA; tel 916-734-5390.

OCTOBER 22–24, 1999: Clinical Endocrinology for Primary Care Physicians. Tropicana, Las Vegas, NV. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; tel 800-421-3756; fax 303-798-5731.

RADIOLOGY

SEPTEMBER 25-26, 1999: Ultrasound Update, 1999. UC Davis at Hilton Hotel, Sacramento, CA. Contact: UCD; tel 916-734-5390.

RESPIRATORY

AUGUST 6-8, 1999: Managing Respiratory Disease. Monterey, CA. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; tel 800-421-3756, fax 303-798-5731.

SURGERY

JUNE 23-26, 1999: 16th Annual San Diego Shoulder Arthorscopy/Autoclasty Course. Tri City Medical Center at Hyatt Regency La Jolla. 28.25 hours. $1650. Contact: Rebecca Quiring, Course Coordinator, 3905 Waring Road, Oceanside, CA 92056; tel 760-940-2066.

GENERAL/MULTIDISCIPLINARY

JUNE 22–29, 1999: Wellness in Practice—Mindfulness-Based Stress Reduction in Mind/Body Medicine. Enloe Medical Center at Mana L'ea Retreat Center, Maui. Contact: Maui Stress Reduction Retreats, Steve; tel 530-898-1495.

AUGUST 24–25, 1999: BLS Instructor Course. American Heart Association at San Leandro. 11 hrs. Contact: CPR Seminars; tel 925-754-7900.

OCTOBER 15–17, 1999: Physician Leadership Program. California Academy of Family Physicians at Laurel Heights Conference Center, SF. 20 hrs. $1245–$1395. Contact: Laura Johnson Morasch; tel 415-394-9121. Web: www.familydocs.org/ Orgs?hcli.html (e-mail: HCLI@familydocs.org).

GENERAL

OCTOBER 1-4, 1999: Converse in Spanish. Maricopa Health System at Scripps Memorial, San Diego. 36 hrs. $695. Contact: Rios Associates; tel 619-218-4875.

OCTOBER 21-25, 1999: Masters of Medicine 1999. Continuing Medical Education Associates at Maui Marriott, Maui HI. 30 hours. $795. Contact: CMEA, P.O. Box 57072, Irvine, CA 92619-7072; tel 800-447-4474 or 949-250-1008; fax 949-250-0445.

JUNE 22-23, JULY 10-11, SEPTEMBER 23, OCTOBER 11-12, NOVEMBER 9, 1999: ACLS Provider/renewal. $115. Information: CPR Seminars; tel 925-754-7900.

LOSS PREVENTION

SEPTEMBER 22–25, 1999: Legal Issues in Damaged Brain Injury Cases. Westin St. Francis Hotel, San Francisco, CA. Contact: tel 916-734-5390.

HOME STUDY/SELF ASSESSMENT

California Physicians' Legal Handbook Series. California Medical Association. Contact: CMA, P.O. Box 7690, San Francisco 94120-7690; tel 800-882-1262.

Breast Cancer, Early Detection and Control. Texas Medical Association. CD ROM. $70. 2 hrs. Contact: Texas Medical Association; tel 800-880-1300; http://www.texmed.org/health_science/hs_poep.html.

COLORADO

To list CME programs here, please send information at least two months in advance to: Mr Robert L. Kennedy, Denver Medical Society, 1850 Williams Street, Denver, CO 80218; or phone 303-377-1850. Brochures, course information, and registration forms are available from the contact person or organization.

TUESDAY NOON CONFERENCES: Various Topics in Medicine. Lutheran Medical Center, Wheat Ridge. Contact: Jean A. Kline; tel 303-425-2951.

FIRST WEDNESDAY OF EACH MONTH: Various Topics in Neurology. Colorado Society of Clinical Neurologists. Contact: Colorado Society of Neurologists; tel 303-449-3566.

SECOND WEDNESDAY OF EACH MONTH: Cardiovascular Education Series. St Anthony Hospital at St Anthony Hospital, Denver. Contact: Rose Powell; tel 303-629-3678.

JUNE 24-26, 1999: Clinical Endocrinology for Primary Care Physicans. Sonesta Beach Resort, Bermuda. Fee $375. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; tel 800-421-3756 or 303-798-9682; fax 303-798-5731.

JUNE 25-27, 1999: Coronary Heart Disease Update. Sheraton Fiesta Beach Resort, S. Padre Island, TX. Fee $375. Contact Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; tel 800-421-3756 or 303-798-9682; fax 303-798-5731.

CONTACT INFORMATION

U of Colo—Contact: University of Colorado Health Sciences Center, School of Medicine, Office of Continuing Medical Education, 4200 E 9th Ave, Denver 80262. Phone 303-372-9050 or 800-882-9153; fax 303-372-9065.

IDAHO

To list CME programs here, please send information at least two months in advance to: Ada County Medical Society, Inc. 305 W. Jefferson, PO Box 2668, Boise, Idaho 83701. Phone 208-336-2930. Brochures, course information, and registration forms are available from the contact person or organization.

JUNE 10-12, 1999: 22nd Annual Snake River Medical Forum. St. Joseph Regional Medical Center at Red Lion Hotel, Lewiston, ID. Contact: Koleen Wagner; tel 208-799-5460.

NEW MEXICO

Information, requests for accreditation, and items to be listed should be sent to the chair of the CME Committee, New Mexico Medical Society, 7770 Jefferson, Suite 400, Albuquerque, NM87109, at least two months in advance. For information on CME accreditation or on the CME requirements of the New Mexico Board of Medical Examiners, please write to the above address or phone 505-828-0237.

NOTE: Course information in the following listing is subject to change on occasion. Check with the sponsoring institution for current details.

EVERY FIRST AND THIRD TUESDAY: Building and Implementing Clinical Practice Guidelines at the Point of Care. Contact: Thomas A. Naegele, DO; tel 505-275-7267.

JULY 30–AUGUST 1, 1999: Neurology for the Non-Neurologist. Eldorado Hotel, Sante Fe, NM. CME 11 hrs Category I. Contact: Linda Main, Meetings Coordinator, MER, 1500 West Canal Court, Suite 500, Littleton, CO 80120-4569; tel 800-421-3756; fax 303-798-5731.

AUGUST 14, 1999: Tenth Annual Update in Primary Care. New Mexico Hispanic Medical Association at the Crowne Plaza Hotel, Albuquerque, NM. Contact: Kelly Little; tel 505-828-0237; fax 505-828-0336.

OCTOBER 7-9, 1999: Santa Fe Colloquium on Cardiovascular Therapy—Can Coronary Artery Disease be Stabilized or Reversed? What About Primary Prevention? American College of Cardiology at Eldorado Hotel, Santa Fe, NM. 17 Cat I hrs. Contact: Registration Secretary, Extramural Programs Dept., American College of Cardiology; tel 800-253-4636, ext. 695; fax 301-897-9745.

Satellite Courses
Contact: Joe Treat or Jim Cato, Immunization Program. Phone 505-827-2366.

CONTACT INFORMATION
UNMSOM—University of New Mexico School of Medicine, Office of CME, PO Box 713, Albuquerque 87131. Phone 505-277-3942.

UTAH

All courses listed meet the criteria for Category 1 of the Physician's Recognition Award of the AMA. To list AMA Category 1 CME courses, send information at least two months in advance to the Office of Continuing Medical Education, 540 East Fifth South, Salt Lake City, UT 84102; or phone 801-355-7477. For information on CME accreditation, please write the CME office at the above address. NOTE: Course information in the following listing is subject to change on occasion. Check with the sponsoring institution.

MEDICAL GRAND ROUNDS

WEEKLY: Grand Rounds in Internal Medicine, Psychiatry, OB/GYN, and Pediatrics. Contact: UUSM.

WEEKLY: Pediatric Grand Rounds. Contact: PCMC.

WASHINGTON

The listing of continuing medical education programs in Washington state is compiled by the Washington State Medical Association. To list Category 1 programs here, please send information at least two months in advance to Continuing Medical Education, Washington State Medical Association, 2033 Sixth Avenue, Suite 1100, Seattle, WA98121; phone 206-441-9762 or 800-552-0612.

Brochures and registration forms are available from the contact person or organization listed at the end of each course or in the list of course sponsors and contact information.

COURSE SPONSORS AND CONTACT INFORMATION
CME HARBORVIEW Contact: Gayle Splater, Cytology Continuing Education, Dept. of Pathology, Harborview Medical Center, 325 Ninth Ave, Seattle, WA 98104. Phone 206-223-5953.
PCMS CME Contact: Executive Director, College of Medical Education, 705 S Ninth, No. 203, Tacoma, WA 98405. Phone 206-627-7137.
U/W (UNIVERSITY OF WASHINGTON) Contact: U/W School of Medicine, Div. of CME, SC-50, Seattle, WA98195. Phone 206-543-1050.
VMMC (VIRGINIA MASON MEDICAL CENTER) Contact: Linda Orgel, Division of Continuing Medical Education, Virginia Mason Medical Center, PO Box 900, Seattle, WA 98111. Phone 206-340-2058.
WSMA (Washington State Medical Association) Contact: Continuing Medical Education, 2033 Sixth Ave, Ste 1100, Seattle, WA 98121. Phone 206-441-9762.

WYOMING

All courses meet the criteria for Category 1 of the Physician's Recognition Award of the AMA. To list AMA Caegory 1 CME courses here, send information at least two months in advance to the Medical Education Committee, Wyoming Medical Society, P.O. B ox 4009, Cheyenne, WY 82009; e-mail skeefe@wyomed.org. Phone 307-634-2424; fax 307 632-1973.

JULY 20-23, 1999: Occupational and Environmental Medicine in Primary Care. Rocky Mountain Center for Occupational and Environmental Health at Jackson Hole, WY. Contact: Registration Coordinator, The Rocky Mountain Center for Occupational and Environmental Health; tel 801-581-5710.

AUGUST 30-SEPTEMBER 1, 1999: Tutorial in the Tetons. American College of Cardiology at Jackson Lake Lodge, Moran WY. 14.5 CME. Contact: Registration Secretary, Extramural Programs Dept., American College of Cardiology, 9111 Old Georgetown Rd., Bethesda, MD 20814-1699; tel 800-253-4636, ext. 695; fax: 301-897-9745.

OTHER CME OPPORTUNITIES

Brochures and registration forms are available from the contact person or organization listed at the end of each course or in the list of course sponsors and contact information.

JULY 18-21, 1999: Eighth National Alzheimer's Disease Education Conference. Alzheimer's Disease and Related Disorders Association at Long Beach Convention Center, Long Beach, CA. Contact: Nicolle Heller, Alzheimer's Association; tel 312-335-4037; Nicolle.Heller@alz.org.

SEPTEMBER 30- OCTOBER 2, 1999: 7th Annual Conference on Management of the Tinnitus Patient. University of Iowa College of Medicine at Medical Alumni Auditorium, Room E331 UIHC, The University of Iowa Hospitals and Clinics, Iowa City, IA. Contact: Cheryl Schlote; tel 319-384-9757; fax 319-353-6739; cheryl-schlote@uiowa.edu.

Guidelines for Authors

Our readers represent all disciplines of medicine, but principally primary care physicians. We aim to publish manuscripts that are reliable and lively and that will improve the care of patients, the health of the public, or policies affecting either. Manuscripts should be of interest to a broad range of busy practitioners, physicians in training, and anyone who has an interest in quality health care. The purpose of a paper or letter may be to report, inform, alert, review, and discuss, but, above all, to teach. We aim to give quick and informative decisions on the articles we receive.

Manuscript submission information

Manuscripts should be sent to:
Managing Editor, Catherine Nancarrow,
WJM Western Journal of Medicine,
221 Main Street, PO Box 7690,
San Francisco, CA 94120-7690;
wjmsf@pacbell.net.

Manuscripts may be submitted via e-mail, but must include print mail address and phone and fax numbers of the correspondent.

Manuscripts must be original, not previously published, and not under consideration by another publisher. If preliminary data were included in another presentation or publication, this should be noted in the cover letter and a copy of that publication should be included.

Any conflict of interest, actual or potential, should be revealed to the Editors (see Letter of Transmittal). Research or project support should be included as a footnote to the manuscript and detailed in the Letter of Transmittal. Obtaining informed consent to protect patients' rights to privacy should be documented according to URM 1997.

All manuscripts should be double-spaced and, including references and abstract but not tables, should not exceed:

- **Original articles:** 2,500 words with a maximum of five tables and 30 references; structured abstract
- **Topics in Review:** 1,500 to 2,000 words with a maximum of 25 references; summary points†
- **Topics for Best Practice:** 2,000 words
- **Evidence-Based Case Reviews:** 2,500 words with two tables and/or figures; summary points†
- **Commentaries:** 600-800 words
- **Letters to the Editor:** 500 words

Structured abstracts

Manuscripts, except for case-based reviews, should include a structured abstract of no more than 250 words with the headings: objectives, design, setting, subjects, interventions, main outcome measures, results and conclusions.

Evidence-based case reviews

Interesting cases presented in an evidence-based, case-based review format provide readers with information and guidance with respect to clinically relevant choices made by practitioners—from diagnostic methods to conclusions as to what might have been done differently given the outcome. Topics to address include:

- epidemiology
- differences in demographic groups
- an evidence-based approach to diagnosis, management, and therapeutics; ethical issues
- cost/economic issues; when to involve a specialist
- what research is needed in the area.

Use of diagrams, tables, and algorithms is highly recommended. Authors should include 5-7 bulleted summary points for a busy primary care provider.

Letters to the editor

Letters must be double-spaced and will be published at the discretion of the Editors. They may be edited for style and brevity. Those of a scientific nature may be subject to peer review.

Letter of transmittal

All authors must sign the letter of transmittal, with one author designated as correspondent and his or her name, address, and telephone and fax numbers included.

A letter of transmittal, except for one accompanying a manuscript from US government employees whose work was done as part of their official duties, must include:

- a paragraph that **transfers copyright:** "In consideration for reviewing and editing my submission, the author(s) undersigned hereby transfers, assigns, or otherwise conveys all copyright ownership to *WJM Western Journal of Medicine,* in the event that such work is published by the journal."
- a statement of **author responsibility** signed by all authors: "I have participated in the conception and design of this work and in the writing of the manuscript and take public responsibility for it. I have reviewed the final version of the

manuscript and approve it for publication. I attest to the validity and legitimacy of data in the manuscript and agree to be named as the lead author or coauthor of the manuscript."

- a description of **sources of funding and the role of sponsors,** including their involvement, if any, in review and approval of the manuscript for publication.
- a statement of **financial disclosure:** "I warrant that I have no financial interest in the drugs, devices, or procedures described in the enclosed manuscript (except as disclosed in the attached statement)."
- a statement that all human subjects involved in experimental investigation gave their **informed consent** and that approval was obtained from the appropriate institutional review board.

Editorial review

All manuscripts are subject to peer review in addition to review by the Editors to determine the originality, validity, and importance of content and conclusions. *WJM* aims to introduce an open peer review system; reviewers' comments may be signed. Reviewers are required to state all possible conflicts of interest.

All accepted manuscripts are subject to copyediting. The corresponding author receives edited page proofs for approval and minor changes and is responsible for clearing all corrections and changes with coauthors.

Manuscript preparation

All manuscript materials, including references, tables, figure legends, and abstracts, must be double-spaced.

Please submit the following:

- The original manuscript, two copies, and a copy of the manuscript (including references, tables, and figure legends) on disk (formatted for a PC/Windows platform and labeled with the word processing program used). Allow a margin of 2.5 to 4 cm (1 to 1.5 in) on both sides.
- Figures, black and white or color, in triplicate unmounted 12.7 × 17.8 cm (5 × 7 in) glossy prints (and transparencies for color figures) with the figure number, lead author's name, and top of the photo indicated with a label on the back.

WJM encourages the use of illustrations and asks authors to submit photographs for publication. When possible, patients should be asked to sign consent forms before pictures of them are published. This should be clearly stated and proof submitted with the manuscript. If obtaining consent is not possible, the reason should be stated in the cover letter. Changing the data on patients should not be used as a way of securing anonymity.

Figure legends, to be typed in sequence on the same page, should be in complete sentences. A letter of permission to borrow from the copyright holder (the previous publisher) must accompany any figures or tables previously published. The permission of the authors should also be obtained. The Editors discourage the use of borrowed figures or tables.

Reprints

A form for ordering reprints will be sent to the corresponding author when the article is published.

References

All references should be cited in the text using superscript numbers and listed in their order of citation. Reference style should follow guidelines adopted by the US National Library of Medicine. The title of the article, name of publication, year of publication, volume number, and first and last page numbers should follow the authors' names.

Journal articles

Abbreviations of journal titles should conform to those used in Index Medicus. List up to six authors; for seven or more, use et al after listing the first six.

Vega KJ, Pina I, Krevsky B. Heart transplantation is associated with an increased risk for pancreatobiliary disease. *Ann Intern Med* 1996; 124:980-982.

Books

Ringsven MK, Bond D. *Gerontology and Leadership Skills for Nurses.* 2nd ed. Albany (NY): Delmar Publishers; 1996.

Personal communications and unpublished data

The use of "personal communication" or "unpublished data" should be avoided and should not be included in the reference list.

For further information

Questions regarding the Guidelines for Authors may be directed to the Managing Editor in writing at the address above or by telephone 415-974-5977, fax 415-882-3379, or e-mail (wjmsf@pacbell.net).

Author checklist

- Original double-spaced manuscript and two copies, as well as PC-formatted disk.
- Illustrations, glossies and/or transparencies, identified with lead author's name, plus figure legends that describe fully and in complete sentences what the figure depicts.
- Letter of transmittal that includes release of copyright, statement of conflict of interest, funding source(s), and authorship responsibility, signed by all the authors.
- A 250-word structured abstract.
- Title page that includes current affiliation of all authors and all contact details for the corresponding author (street and e-mail addresses, phone numbers, fax numbers).
- Permission-to-borrow letters for any previously published illustrations or tables.
- Informed consent obtained.

Uganda, May 1983—

Immunization, Tororo region.

see text p.383

David Heiden

David Heiden is an ophthalmologist practicing in San Francisco.

For reprints opportunities, please contact:

Marsha Fogler

Tel: 1(800) 482 1450 or 1(609) 482 9665 Fax: 1(609) 482 7414

Email: fogler@erols.com

Specialist Journals from BMJ Publishing Group
Live and Online
Now on a screen near you
Free until July 1999
Full text
Fully searchable archive
Articles collected by topic
Customised email alerts
Direct Access to Medline
eHEART www.heartjnl.com
NOW ONLINE
eJNNP www.jnnp.com
NOW ONLINE
eBJO www.bjophthalmol.com
NOW ONLINE
eGut www.gutjnl.com
NOW ONLINE
eThorax www.thoraxjnl.com
NOW ONLINE
eARD www.annrheumdis.com
NOW ONLINE
eADC www.archdischild.com
NOW ONLINE
BMJ Publishing Group